THE QUARTERLY REVIEW OF BIOLOGY

SEPTEMBER
1955

Vol. 30 No. 3

Published by
THE WILLIAMS & WILKINS COMPANY
BALTIMORE, U. S. A.

Copyright 1955
THE WILLIAMS & WILKINS COMPANY

THE QUARTERLY REVIEW OF BIOLOGY

FOUNDED BY RAYMOND PEARL

B. H. WILLIER, *Editor*
The Johns Hopkins University

H. BENTLEY GLASS
Associate Editor

CARL P. SWANSON
Assistant Editor

Advisory Board

IRVING W. BAILEY ..... *Harvard University*
G. W. BEADLE ..... *California Institute of Technology*
DAVID R. GODDARD ..... *University of Pennsylvania*
ROSS G. HARRISON ..... *Yale University*
LIBBIE H. HYMAN ..... *American Museum of Natural History*
A. L. KROEBER ..... *University of California*
K. S. LASHLEY ..... *Harvard University*
CHARLES W. METZ ..... *University of Pennsylvania*
THOMAS PARK ..... *University of Chicago*
ALFRED S. ROMER ..... *Harvard University*
ALEX G. RUTHVEN ..... *University of Michigan*
F. O. SCHMITT ..... *Massachusetts Institute of Technology*
PAUL WEISS ..... *Rockefeller Institute*

Papers to Appear in an Early Number

PROBLEMS IN INVERTEBRATE CHEMORECEPTION
Edward S. Hodgson, *Barnard College and Columbia University*

THE PHYSIOLOGY AND HISTOLOGY OF THE CONTACT CHEMORECEPTORS OF THE BLOWFLY
V. G. Dethier, *The Johns Hopkins University*

Entered as second-class matter January 27, 1926, at the post office at Baltimore, Maryland, under the act of March 3, 1879. Subscription price $6.00 a year ($6.75 outside U.S.A., except Canada. Canada, $6.25) $1.75 a single copy, when available, $.25 postage outside U.S.A.
Made in United States of America

EXPERIMENTAL DESIGN:
Theory and Application

BY WALTER T. FEDERER

Professor of Biological Statistics, Cornell University

The central plan of this book is to discuss the advantages, the disadvantages, the experimental lay-out, and the analysis for each design. The author says in the *Preface*: "Facts concerning experimental design are scattered throughout statistical literature. . . . The basic reason for writing this book was to present subject matter and techniques not available in other texts."

To be published late Fall 1955

GENERAL BIOLOGY,
FOURTH EDITION

BY JAMES W. MAVOR

Professor Emeritus of Biology, Union College

Noted for its good balance between the "type" and "principles" approach since its first publication in 1936, a reviewer says: "This fourth edition of a popular biology text is offered with the general plan of previous editions retained but recent information included in many chapters. A considerable number of new illustrations have been added. The book should continue to serve as an excellent introductory text to the general biology student." From the AIBS Journal. *1952 875 pages $6.50*

HUMAN PHYSIOLOGY

BY W. B. YOUMANS

Professor of Physiology, University of Wisconsin

A concise but full coverage of human physiology for college students who have had either no college science or just one course in general chemistry, general zoology, or both, this text features numerous descriptions of actual experiments that enable learning by example. A complete consecutive treatment of the subject, the text also includes background material in related sciences, methods, and more advanced topics. *1954 481 pages $6.00*

The Macmillan Company

60 FIFTH AVENUE, NEW YORK 11, N.Y.

(In writing to advertisers, please mention the journal—it helps.)

Annals of Human Genetics

(FORMERLY ANNALS OF EUGENICS)

Edited by L. S. PENROSE *with the assistance of*
JULIA BELL, R. A. FISHER, J. B. S. HALDANE, MARY N. KARN, R. R. RACE, J. A. F. ROBERTS AND C. A. B. SMITH

Vol. XX. Part 1. August 1955.

CONTENTS

On the inheritance of muscular dystrophy. J. N. WALTON
With a note on the blood groups by R. R. Race, and a note on colour vision. U. PHILIP
The familial distribution of congenital tritanopia. H. KALMUS
Phenotypes and genotypes in cystinuria. H. HARRIS, U. MITTWOCH, E. B. ROBSON AND F. L. WARREN.
Reviews

The Editor regrets that owing to recent increases in the cost of production it is necessary to raise the subscription to $11.00 per volume post free. The new price will begin with Volume 20.

NEW ISSUES OF THE GALTON LABORATORY
EUGENICS LABORATORY PUBLICATIONS—MEMOIR SERIES

XXXVI Race crossing in Man. The Analysis of Metrical Characters. By J. C. TREVOR, Ph.D. Price $2.50.

XXXVII An Introduction to Human Biochemical Genetics. By H. HARRIS, M.D. Price $2.75.

Issued by the CAMBRIDGE UNIVERSITY PRESS

32 East 57th Street, New York 22, N. Y.

ECOLOGY

Official Publication of the ECOLOGICAL SOCIETY OF AMERICA
Continuing the Plant World

Editors:
Edward S. Deevey (Zoology), Yale University — **W. D. Billings** (Botany), Duke University

Vol. 36, No 4 — *Table of Contents* — October 1955

Analysis of phytoplankton yields in relation to certain physical and chemical factors of Lake Michigan
Ruth E. Griffith
The fish population of spring-fed swamp in the Mississippi bottoms of southern Illinois
Gerald E. Gunning and William M. Lewis
A prairie continuum in Wisconsin ..... *J. T. Curtis*
Studies on territorialism and sexual selection in dragonflies ..... *Merle E. Jacobs*
Some pollen profiles from Arctic Alaska ..... *D. A. Livingstone*
Mortality of oysters and abundance of certain associates as related to salinity ..... *Gordon Gunter*
Phytosociological and environmental characteristics of some plant communities in the Umiat region of Alaska
Ethan D. Churchill
Regulatory mechanisms of house mouse populations: social behavior affecting litter survival
Charles H. Southwick
The interrelations of littleleaf, site index, soil, and ground cover in Piedmont shortleaf pine stands
Otis L. Copeland, Jr., and Robert C. McAlpine
The factor of topographical cues in bird homing experiments ..... *W. E. Arnould Taylor and A. M. Malewski*
Deciduous forests of Ponemah Point, Red Lake Indian Reservation, Minnesota
Murray F. Buell and F. H. Bormann
The spider population of the abstract broomsedge community of the southeastern Piedmont
Robert D. Barnes and Betty Martin Barnes
Root systems of some chaparral plants in southern California
H. Hellmers, J. S. Horton, G. Juhren, and J. O'Keefe
A field study of the activity of the mole (*Talpa europaea*) ..... *Gillian K. Godfrey (Mrs. Crowcroft)*
The vegetational structure of an abandoned field in southeastern Michigan and its relation to environmental factors ..... *Francis C. Evans and Eilif Dahl*
Some aspects of habitat selection and other behavior of cavern-dwelling bats ..... *John W. Twente, Jr.*
Heterotheca latifolia, a new and aggressive exotic dominant in Piedmont old-field succession ... *Catherine Keever*
A resting stage without encystment in the life cycle of the freshwater copepod, *Cyclops strenuus strenuus*
Kare Elgmork
Some effects of meteorological factors on all stages of *Aphytis* "A," a parasite of the California red scale
Paul DeBach, T. W. Fisher, and John Landi
NOTES AND COMMENTS — BOOK REVIEWS

Orders should be placed with
Duke University Press
College Station, Box 6697 — Durham, North Carolina

(In writing to advertisers, please mention the journal—it helps.)

VOL. 30, NO. 3 September, 1955

THE QUARTERLY REVIEW of BIOLOGY

THE ETIOLOGY OF CROWN-GALL

BY RICHARD M. KLEIN
The New York Botanical Garden
AND
GEORGE K. K. LINK
The University of Chicago

This review is dedicated to the memory of Dr. Erwin Frink Smith (1854–1927), who was in charge of the Laboratory of Plant Pathology, Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., and who blazed the trails in the study of crown-gall and of bacterial diseases of plants in general.

INTRODUCTION

CROWN-GALL is the collective name for the neoplastic swellings (Fig. 1) formed on susceptible plants following their infection with the schizomycete, *Agrobacterium tumefaciens* (Smith and Town) Conn., and for the symptom complex (Figs. 2, 3) in other parts of the affected plant which may accompany development of these tumorous growths. The collective syndrome of crown-gall is a highly complex one which includes the diverse behaviors of many species of plants in the presence of different strains of inciting bacteria. In this review, the term etiology is used not only with reference to the inciting bacteria but in its broad sense to designate the body of knowledge dealing with all the antecedents of the initiation and development of the crown-gall syndrome.

The review is grounded on the proposition that each event or process in crown-gall, as in most other bio-events, arises out of a causal complex, each component of which is a necessary, but not a sufficient, cause of the event or process under consideration (Link, 1932; Link, Wilcox, and Link, 1937). In so far as an event or process is not of spontaneous, intrinsic origin, it is a change or *affect* produced by something, the affectant or affector, acting on the affected or affectee. The affectant and the affectee may each be a substantial thing, a state, a condition, or a process. The change under way on or in an affectee while it is being acted on by the affectant is an affect or affection in a limited sense of the term (= Gr. *pathos*, Lat. affectio, passio). The direct, immediate result of the affect, when the affector has ceased its activity, is the direct immediate *effect* of the affect. In case of a progressive and/or cumulative result, each such result, too, is a direct, immediate effect, terminating in the final, end effect. The direct, immediate effect may lead to a secondary affect with its effect, a secondary to a third, and so on, producing a more or less temporarily extended chain of affects and effects comprising the initial or primary direct affect and its effect and the subsequent indirect affects and effects.

A change, elicited by an affect or effect or by an affectant in the affectee is a passive or active response-affect or response-effect. If it counters the affect or effect or the affectant which elicits it, is a counter-affect or counter-effect. If it is an active counter-affect or effect, it is a counter-

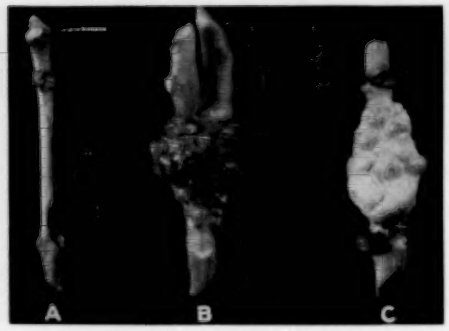

FIG. 1. THE ROLE OF GENETIC FACTORS IN THE DISPOSITION OF PLANTS TO DEVELOP CROWN-GALL, SHOWN IN THE DIFFERENTIAL RESPONSES OF A, BEAN, B, TOMATO, AND C, BRYOPHYLLUM, TO INOCULATION EACH IN THE COMPARABLE INTERNODE WITH *AGROBACTERIUM TUMEFACIENS*

Galls of bean and tomato have ceased growth while that of *Bryophyllum* still is very active, with a light colored surface due to deficiency of development of chloroplasts. The surfaces of the bean and tomato gall have become brown and necrotic. The galls are six weeks old and developed simultaneously at the same temperature in moderately moist air. × ½. From Link, Wilcox, and Link, 1937.

active affect or effect, i.e., a reaction in the strict sense of the term as used by pathologists.

An affect and effect may occur at any level of bio-organization, ranging from whatever is the currently considered lowest level (at present a gene, virus, or desoxyribosenucleic acid) to the most complicated human social organization. The affect may be a change in the material, the dynamic, or the relational characteristics of the affectee.

The causal complex of the affect always includes the usual readiness or disposition or the unusual readiness or predisposition of the affectee to be acted upon or affected, as well as the action of the affectant on the affectee at the site and moment under consideration. The effect also arises out of the readiness or nonreadiness of the affected for passive or active changes, or both, in the presence of and following the affect. Generally, the causal complex of readiness or nonreadiness of the affectee to be affected and to manifest an effect, and of the affectant to act, affect, or be effected comprises both intrinsic and extrinsic factors and agents. Relative to an affected plant in which crown-gall occurs, the category of intrinsic factors comprises hereditary factors, internal environmental factors, i.e., other parts of the whole acting on the part under consideration, and past history factors, i.e., the cumulative effect of the affects of all prior causal complexes in the subject under analysis. Relevant to the affected plant or any of its parts, the category of extrinsic factors comprises all pertinent external non-living and living factors and agents. The bacterium and its products belong to this category. The causal complex of the readiness or nonreadiness of the bacteria to act at a particular site at any given moment and to be affected includes intrinsic (hereditary, past history, etc.) factors as well as extrinsic environmental factors or agents, including the host.

Link (1932, 1933) pointed out that etiological analysis of a complicated overall event or process often is facilitated by conceptually cutting the total event into a close series of contiguous time slabs or part events, in which each preceding part event stands in causal relation to subsequent events. Thus, a crown-gall tumor is the manifestation of an overall process which begins with an initial event and leads into a train of subsequent events.

Several investigators have recognized part events in the formation of a crown-gall tumor. Levin and Levine (1920, 1922) and Levine (1936, 1947) suggested that, in vivo, all crown-gall tumors pass through stages in a life cycle with a latent period and periods of active growth, maturation, senescence, necrobiosis, and necrosis. Braun and Laskaris (1942) recognized two phases in tumor formation, the first characterized by alteration of a normal into a tumor cell, the second by stimulation of the altered cell to continued multiplication resulting in tumor formation. Later, Braun (1954b) recognized two phases in the alteration of a normal cell, conditioning and induction, which eventuated in a tumor cell. This cell, if not properly stimulated, does not divide, but if properly stimulated, gives rise to a detectable tumor by cell division. Klein (1952) and Klein and Link (1953) delimited three periods of cellular change and behavior: a period of cellular transformation, a period of cellular duplication, and a period of cellular differentiation and organization. Klein (1954) modified this scheme to include four phases of cellular change during the period of cellular transformation.

This review recognizes four stages in a life history of a crown-gall tumor: initiation, growth, maturation, and senescence and death. Each of these stages is characterized by a particular type of cellular change and behavior or by a dominance of one type. Four periods of cellular change parallel these stages in the life history of a tumor and are here designated as transformation, duplication,

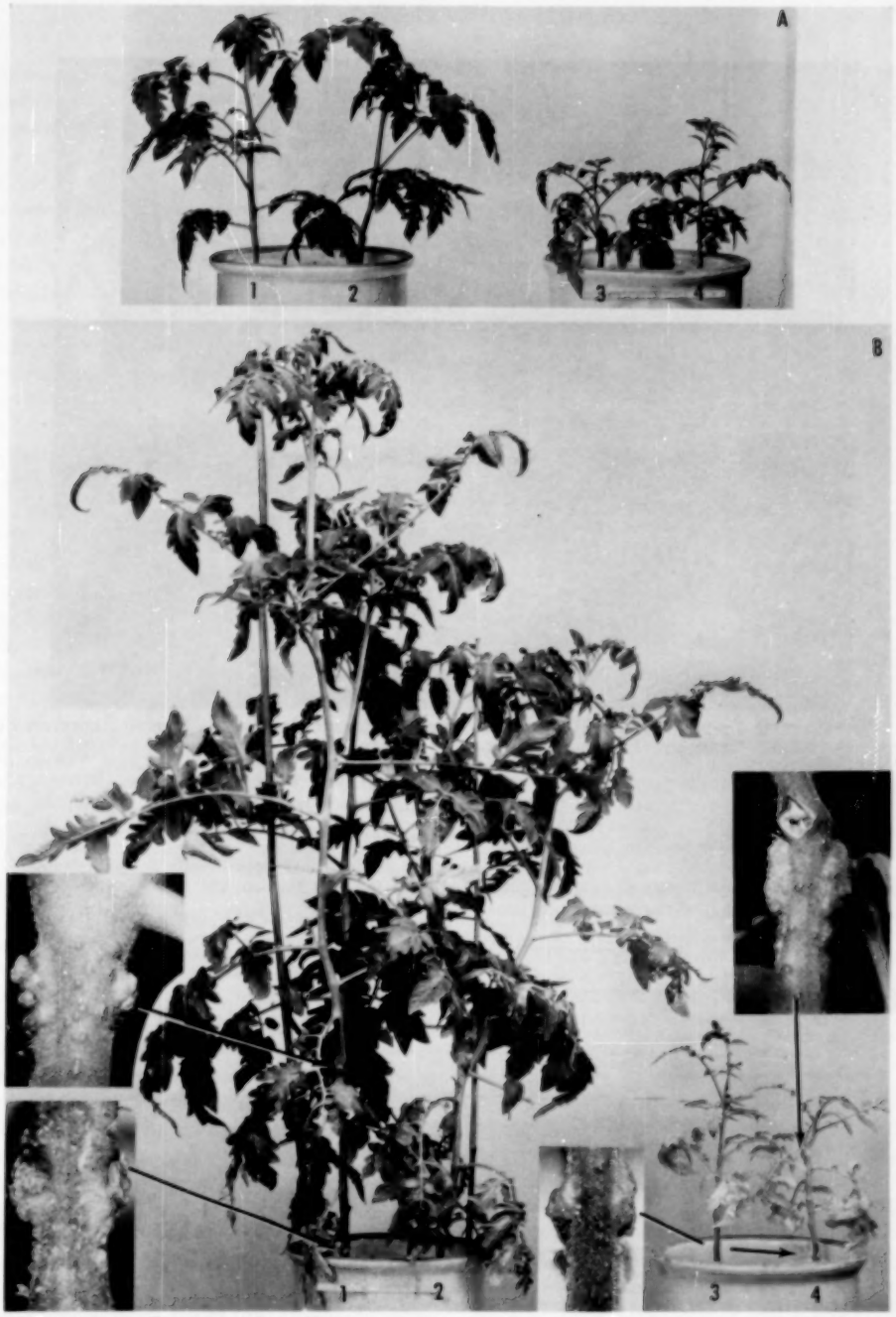

FIG. 2. DIFFERENTIAL EFFECTS OF PAST HISTORY AND INTERNAL ENVIRONAL FACTORS DUE TO RELATIVELY HIGH AND LOW NITRATE NITROGEN NUTRITION, (A) IN STEMS AND LEAVES OF TOMATO PLANTS AND (B) IN RESPONSE OF INOCULATED HIGH-NITROGEN AND LOW-NITROGEN PLANTS TO *AGROBACTERIUM TUMEFACIENS*

A, fifteen-week-old plants. Plants 1 and 2 (high-N) were succulent, dark green; plants 3 and 4 (low-N) showed early symptoms of nitrogen deficiency, with lessened growth, yellow-green color, and decreased succulence. B, same plants as in A, at same scale, 51 days after inoculation. High-N plants still were growing, were succulent, green, and flexible, whereas low-N plants were stunted, woody, yellow, and rigid. Insert, photographs of resultant tumors of plants 1 and 4 to the same scale. From Link, et al., 1953.

FIG. 3. DIFFERENTIAL EFFECTS OF PAST HISTORY AND INTERNAL ENVIRONAL FACTORS DUE TO RELATIVELY HIGH AND LOW NITRATE NITROGEN NUTRITION ON (1) ENTIRE PLANTS OF THE SAME GENETIC CONSTITUTION GROWN SIMULTANEOUSLY UNDER OTHERWISE IDENTICAL EXTERNAL ENVIRONAL CONDITIONS OF LIGHT, TEMPERATURE, AND HUMIDITY, (2) RESPONSES OF THE HYPOCOTYL OF THESE PLANTS TO INOCULATION WITH *AGROBACTERIUM TUMEFACIENS*, AND (3) THE EFFECTS OF THE TUMOR ON THE TUMOR-BEARING PLANTS

The low-N plants (A) were stunted, woody, yellow, and rigid, and the tips of the remaining leaves had begun to die. The high-N plants (B) were succulent, green, and flexible. The lower leaves of the high-N inoculated plants show epinasty. Both low-N and high-N inoculated plants show adventitious roots directly below the tumor. Absolutely, the tumor of the low-N plants is almost as large as that of the high-N plant, and, relative to weight of entire plant, it is larger than that of the latter. From Link, et al., 1953.

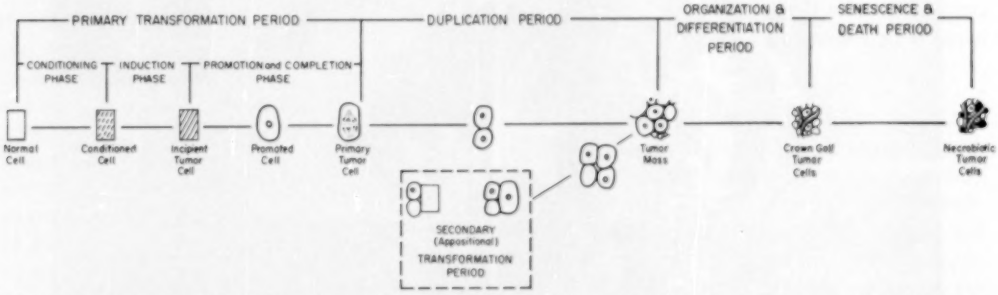

FIG. 4. DIAGRAMMATIC REPRESENTATION OF THE PERIODS AND PHASES OF CELLULAR CHANGE AND BEHAVIOR IN THE GENESIS OF A CROWN-GALL TUMOR

differentiation, and necrobiosis and death. The time intervals during which these cellular changes occur have been given the same designations (Fig. 4).

Transformation is defined as the sequence of events occurring in an initially normal cell and leading to its alteration into a tumor cell. A tumor cell, accordingly, is a cell which has experienced such transformation or the immediate or distant progeny of such a cell, and a crown-gall tumor consists of tumor cells and, probably, of occluded non-tumorous cells. A transformation which results in a population of infrequently dividing descendants of the tumor cell with resultant small

tumors may be designated as a minimal transformation, while one which brings about a population of frequently dividing progeny of tumor cells, with resultant large tumors, may be termed a superminimal transformation, or, at best, an optimal transformation. Two kinds of transformation may occur, primary and secondary. Primary transformation is effected by crown-gall bacteria, while secondary transformation is brought about by agents and factors different from those active in primary transformation. In this review, a cell which has undergone primary transformation or is a descendant of such a cell is designated a "primary tumor cell," and a cell which has undergone secondary transformation or its progeny is termed a "secondary tumor cell." This distinction is necessary because some cells in a primary tumor may be secondary tumor cells. Smith (1911) called the tumor which arises at the site of inoculation the primary tumor and one which develops distant from that site, a secondary tumor (Fig. 5). The situation has been complicated by the finding that some secondary tumors (according to Smith's definition), arose from cells which had undergone primary transformation. Furthermore, even a primary tumor may arise from cells which had undergone secondary as well as primary transformation.

This review will deal seriatim with the etiologies of the phases of cellular changes which characterize the primary or secondary transformation period and those cellular changes which occur during the subsequent periods of cellular change and behavior in the life history of a tumor. Structure and form, activities, composition, relations, and products of the cells pertaining to each phase and period of cellular change and behavior, as well as distant changes in the host plant resulting from these cellular activities, are discussed because they are considered part of the causal complex of the stage under consideration and are components of the causal complex of subsequent phases or periods in tumor genesis.

After this review had been completed, Link inclined to accept the conclusion of Braun and Laskaris (1942) that induction completes alteration of a normal into a tumor cell. This implies that what is here considered an "incipient tumor cell" is a tumor cell, and that what is here considered promotion and completion of an incipient tumor cell into a tumor cell is stimulation of a tumor cell to enlarge and divide. If this proposition is accepted, Link proposes that the Duplication Period

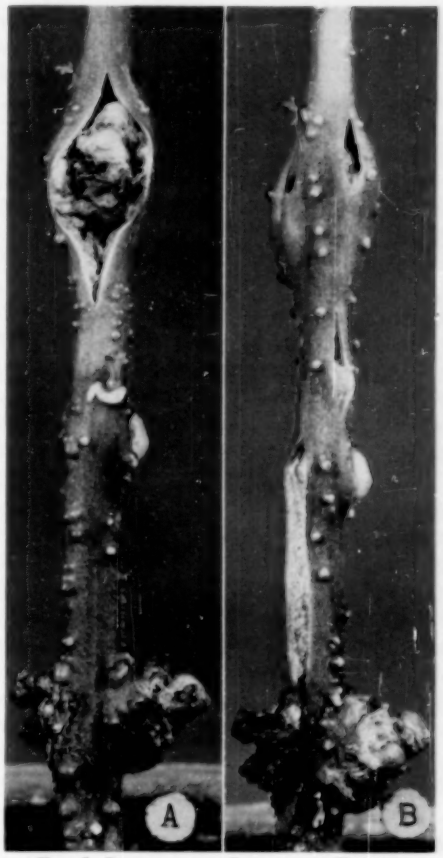

FIG. 5. PRIMARY AND SECONDARY TUMORS

Front (A) and rear (B) view of basal portion of stem of tomato plant grown in soil and inoculated only at site of basal tumor by puncture completely through the internode, when elongation of internodes shown had ceased. Histological examination revealed no tumor strands between the primary and secondary tumors. Reproduced from Link et al., 1953.

be considered to comprise two phases of cellular change—a Cell Stimulation and Cell Enlargement Phase and a Cell Division Phase. This change of Link's interpretation resulted from Braun's finding that what is here designated the incipient tumor cell may remain disposed to stimulation for as long as six weeks. According to the interpretation presented in this review this is a delay of the promotion and completion phase of the Primary Transformation Period, while according to Braun, it is a delay in stimulation of the transformed cell to divide. This change of view is also due to the findings of Skoog (1950, 1954) and others relative to the action and role of attenuated bacteria in transformation and stimulation.

INITIATION STAGE OF A PRIMARY TUMOR

Primary Transformation Period

Conditioning Phase

The events leading to the formation of a primary tumor cell in susceptible tissues are initiated by the infliction of a wound with or without the simultaneous introduction of virulent crown-gall bacteria. With the exception of two notes (Stapp, 1925; C. O. Smith, 1944), no reports of tumor induction without initial wounding have appeared. In both of these cases, the authors themselves noted that the experiments were of questionable validity. This necessity for a wound led Smith et al. (1911) to suggest that wounding was necessary to permit the entry of the bacteria into those cells which were to become neoplastic. Smith reported (1912, 1916a) that crown-gall bacteria were intracellular in all tumor tissues and Pinoy (1925) observed the bacteria within large cells associated with the tumor tissues. Riker (1923a), Robinson and Walkden (1923), Magrou (1926), and Nemec (1928) were unable to confirm these observations and conclusively demonstrated that the bacteria were intercellular in tumor tissues and were intracellular only in necrotic cells. Further, since most, if not all, of the injured cells die, it is unlikely that the wound is necessary for endoprotoplasmic insertion of the bacteria. Magnus (1918) and Riker (1923a) reported that the destruction of injured cells by heat did not prevent tumor formation and interpreted this finding as an additional indication of the extracellular site of the bacteria. In fact, the insertion of crown-gall bacteria into single cells on the stems of tomato plants did not result in tumor-cell formation (Hildebrand, 1942). It was suggested by Hildebrand that the living cell-interior is an unfavorable medium for the development of the bacteria.

Several workers then advanced the hypothesis that the wound was required merely to get the bacteria into intimate contact with susceptible cells. By a number of techniques, bacteria were introduced into healthy tissues without wounding the area. Patty (1930), Schmidt (1933), Johnson (1937), and Rack (1953) introduced virulent bacteria into substomatal spaces, or into healthy organs by vacuum infiltration, water soaking, or via the transpiration stream. All of these experiments gave negative results. C. O. Smith (1913), Levine (1920), Riker (1923a), Suit and Eardley (1935), and others found that the bacteria could travel in the vascular tissues throughout the plant without inducing tumor formation. Klein (1954) was unable to induce tumor formation in *Kalanchöe* stems containing bacteria unless a fresh wound was made in the infection court. Rack (1953) infiltrated *Bryophyllum* leaves with bacteria and found that localized application of dry ice, small heat burns, or chemical burns, all of which caused wounding, were each effective in initiating tumor formation. Small tumors occasionally developed on the *Bryophyllum* leaves when the buds in the notches of the leaves started to develop. This type of response was also noted by Klein (1954) in *Kalanchöe* stems when roots developed in the infection court. None of these observations conflict with the wound hypothesis, since tearing of tissues has been shown to accompany both leaf-bud development and the formation of adventitious roots.

In general, wounding plays its etiological role in tumor genesis within the first two to four days after the injury. After that time wound healing begins. Several studies have been made on the length of time a wound site remains predisposed to the effects of crown-gall bacteria. Riker and Keitt (1926), Siegler (1928), and Riker and Banfield (1932) observed that callused apple grafts failed to serve as an open infection court for crown-gall bacteria. Banfield (1934) reported that injured raspberry roots remain susceptible up to seven weeks, but scrutiny of his methods casts doubt on the results. DeRopp (1948a) concluded that callus tissues form a mechanical barrier to the movement of crown-gall bacteria. He (1948c) was able to induce tumor formation in slices of fleshy storage roots by application of bacteria up to one week after injury. In *Vinca rosea*, the processes leading to tumor formation can be accomplished only during the first four days after wounding (Braun, 1947a). Using *Kalanchöe*, Braun and Mandle (1948) found that the host cells were susceptible to alteration just before or during the earliest detectable stages of wound-healing. Klein (1954) found that cells on the surface of bisected stems of tomato could be transformed only during the first two days after injury, a finding in agreement with that of Riker (1923a). Histological examination of the cells on the cut surface showed that susceptibility to tumor formation was lost when wound-healing (cytoplasmic and nuclear basophilia, nuclear enlargement, etc.) became microscopically evident. There is little doubt that species differences exist in the timing of the healing process. Account must also be taken of the ex-

ternal factors, since temperature, relative humidity, light, etc., affect the rates of disappearance of those factors which are involved in wound-healing (Riker, 1923a). It is certain, however, that initiation of the processes of wound-healing modifies the disposition of cells to tumor induction. Success or failure to develop positive predisposition to the action of etiological agents which subsequently are necessary for transformation are functions of the physiological state of the healing tissues.

It seems clear that it is not the wound per se nor the ruptured and dying cells that condition the cells, and attention was therefore focused on the products released from wounded cells. In this connection the scattered references to wounding and wound sap are of considerable interest. Riker (1923a), Hamdi (1930), Levine (1923a), and Hildebrand (1942) made critical studies on the relation of initial wound size to eventual tumor size. They found that although the eventual size of a tumor was unrelated to the number of bacteria comprising an inoculum, one bacterium theoretically (but not actually) being sufficient to initiate tumor formation (Levine, 1923a), the ultimate size of the tumor was usually directly proportional to the severity of the wound. Thus, the more massive the wound, the larger the tumor. In tomato the minimum number of wounded cells required was quite small, but only a small percentage of inoculations involving minute wounds was successful (Hildebrand, 1942). It was suggested that the larger amount of "wound juice" present in large wounds was related to the size of these tumors. Field observations (Sherbakoff and McClintock, 1935) also indicated that only small crown-gall tumors formed following the tiny bites of insects. Smith (1922) believed that the "wet, wounded areas resulting from the tearing of cells" were somehow related to tumor formation, and Riker (1923a) reported that the water-soaked area resulting from the flooding of the intercellular spaces usually delimits the size of the tumor. Hamdi (1930) and Hildebrand (1942) proved that droplets of wound sap inserted into tiny punctures resulted in larger tumors than otherwise would have formed. Klein (1954) found that when cut discs of garden beet root were washed for ten or more hours before inoculation by surface application of the bacteria, no tumors were formed nor did callus form on uninoculated discs. Prior to the limiting time of washing of ten to twelve hours, a proportionality existed between the length of washing time and decreases in tumor or callus formation. The ability of washed beet tissues to initiate tumors or to form callus could be restored completely by application of wound sap to the surface of the disc at the time of inoculation. Traumatin, a reputed wound hormone (Bonner and English, 1938), was without effect on either process. These findings suggested that one result of wounding is the release from, or formation by, ruptured or adjacent uninjured cells of materials which are required for the formation of both tumor and callus cells.

Two other sets of experiments are instructive. Rack (1953) infiltrated *Bryophyllum* leaves with crown-gall bacteria and found that no tumors were formed unless a fresh wound was made into the infection court. Tumors were formed, however, if leaves were infiltrated with wound sap subsequent to the infection with bacteria. Infiltrations of indoleacetic acid were without positive effect. Klein (1954) placed a mixture of wound sap and bacteria on the surfaces of healed discs containing bacteria in situ; this was also followed by tumor formation.

The simplest hypothesis to account for these findings is to assume that materials in the juices of wounded plants play roles in both primary transformation and callus formation and that these roles may be identical for both processes. Certain of the substances in the wound sap of higher plants have been called "wound hormones" (Haberlandt, 1921) and are considered to have many effects on resting cells. Audus (1953) reports that Weisner, more than 50 years ago, suggested that wounded cells might produce a chemical substance that could diffuse into neighboring tissues and evoke a callus-producing response. These effects on cells include respiratory modifications ("wound respiration"), increases in cyclosis, changes in permeability, etc. (Bloch, 1941, 1952), which, under suitable conditions, are etiological factors in cell enlargement, callus and periderm formation, and wound healing. The specific roles of these substances in tumor genesis can only be inferred. In any case, once histologically detectable wound-healing starts, the healing tissues no longer form or release those substances which are required for the conditioning of cells.

Important clues for a specific role of wounding in tumor genesis were found in 1942 by Braun (1952a). He observed that when plant tissues were wounded one day before the introduction of the bacteria, a total time of about thirty-six hours after wounding (an additional twelve hours of bac-

terial contact) was necessary to transform the cells into tumor cells. When the bacteria were introduced at the time of wounding, transformation still required thirty-six hours. Even earlier, Braun and Mandle (1948) suggested that large tumors are initiated when the alteration occurred after the first day following wounding and infection.

In other experiments, Braun (1952a) wounded one set of plants two days before the introduction of the bacteria and another set at the time of inoculation. The bacteria were allowed to act for only twenty-four hours before the transformation processes were stopped. Plants which were wounded before inoculation formed large tumors, while the control plants showed no tumorous reaction. It was also shown that the activities of the host cells attendant upon wounding are not affected by those temperatures which prevent induction processes. Braun also determined that these wounding reactions were time-dependent, the predisposition of the host cells to induction processes (as measured by the tumor size) reaching a maximum within two days. A period of at least six to twelve hours seems to be necessary before the cells become at all susceptible to the action of agents produced by the bacteria-host association. Finally, it was demonstrated that this time effect was not due to the presence of diffusible or soluble substances elaborated by the previously wounded cells. Apparently the effects of the wounding are related to physiological modifications of the healing cells themselves under the influence of wound substances. On the possibility that some special constituent of the conditioned cells was being formed during the two-day conditioning period, a cell-free extract of conditioned tissues was mixed with virulent bacteria and injected into unwounded tissues. Under these conditions the transformation of the resting cells did not occur during a twenty-four hour period, as might have been expected had the wound effects been due to "aging" of the wound sap. Braun pointed out, however, that an "aging factor" might have been inactivated by the techniques used or may be active only within the living cell.

These experiments suggested that wounding reactions essential for conditioning are independent of the presence of the bacteria and that conditioning of cells which are to become tumorous must involve predisposing them to the action of those etiological factors and agents which are formed by the bacterial-host association. Braun (1952a) suggested that the degree of cellular "activation" reached at any given time in the wound-healing cycle is proportional to the concentration and activity of wound substances and that the intervention of normal wound-healing stops the conditioning processes. This may be brought about by the cells ceasing to form or to release the necessary materials. This point will be examined later.

The terms "activation" and "conditioning", however, are not precise expressions of etiological events. They designate those modifications of affected cells which predispose them for subsequent events and processes. These modifications probably include permeability changes (Braun, 1952a), quantitative and qualitative changes in metabolic activity (Klein, 1952), and other alterations, yet unknown. There are no microscopic or cytochemical changes detectable by present methods which distinguish conditioned cells from normal cells (Klein, Rasch, and Swift, 1953).

In summary, the initial cellular events occurring during the Conditioning Phase of primary tumor transformation seem to be those involved in the wounding of the prospective tumorous tissues and their responses to wounding and to the products of wounded cells. The crown-gall bacteria do not seem to be required for any of these processes. Wound substances, possibly including "wound-auxins" released from or formed by ruptured cells, predispose them to the etiological events and processes which occur in subsequent phases of the Transformation Period. This predisposition is not permanent, the conditioned cells becoming callus cells if not acted upon by tumor-inducing agents. Conditioning thus becomes a "past-history factor" which determines the potential range of response of the cell. The conditioning of most plant tissues is sufficiently far advanced within twenty-four hours after injury to predispose the cells to the action of those agents that are operative in the Induction Phase of the Transformation Period.

Induction Phase

Although the presence of virulent crown-gall bacteria is not a necessary part of the conditioning of normal cells, the bacteria are required for the processes and events occurring during the Induction Phase. This fact necessitates some consideration of the bacteria independent of the host and of the effects of the host on the bacteria.

Studies on the structure, physiology, biochemistry, and serology of crown-gall bacteria have been conducted by many investigators. The results

have been summarized by Riker and Berge (1938), Riker, Spoerl, and Gutsche (1946), and by Stapp (1953). In general, virulent bacteria show no special characteristics which are sufficiently well marked to be significant in a priori determination of their capacity to induce primary tumor cells.

Smith (1923) cautioned workers to use only smooth, translucent colonies of crown-gall bacteria for infection tests. Levine (1925) also noted, in passing, that smooth colonies appeared to be most satisfactory for inducing crown-gall. Link and Hull (1927) reported that crown-gall bacteria may form smooth colonies and wrinkled, dry-surfaced, rough colonies on the same medium. The rough colonies frequently developed smooth edges and, within a few days, were entirely smooth. Link and Hull did not test the virulence of their rough and smooth colonies. Quirk (1931) observed that smoothness and roughness of colony form was a function of the pH of the medium, rough colonies being the rule at pH 6.0 and smooth colonies predominating at pH 7.0, with mixed colonies being present at pH 6.5. She reported that only the smooth colonies were virulent. Verona (1942) has made similar statements. One immediately is reminded of the virulence of pneumococci as related to colony form, but the same conditions do not apply. The spontaneous alterations from rough to smooth, the presumed absence of a capsule about the crown-gall bacterium, and other dissimilarities suggest that; if these observations are correct, factors other than a polysaccharide synthesis are operating. This problem has not been solved.

Muncie and Patel (1930), among others, have shown that numerous strains of the crown-gall bacteria exist and that they may be separated on the basis of physiological and biochemical criteria. Stapp (1927) has reviewed the literature dealing with the serological differences among many of these strains. Patel (1927, 1928) stated that virulence could not be detected serologically. Riker and Hildebrandt (1951) recently reviewed the studies bearing on the characteristics of all the bacteria that induce tumor formation. They complicated the problem unnecessarily by using host range as the major basis for taxonomic separation of the bacterial strains and of the tumors induced by these strains. Studies which demonstrate that the property of virulence for specific hosts can be acquired by transmittance of transformation experiments (Klein and Klein, 1953) indicate that precise taxonomic separation of the bacteria on the basis of host range is impossible. There is no doubt that, at least by cultural criteria, the strains remain true to type. Rosen (1926), Paluch (1938), Rybak (1947), and Gainor and Price (1952, 1953) all found that the bacteria are remarkably stable.

Several workers (Demaree and N. R. Smith, 1952: Coleman, 1950a; McKeen, 1954a, b) were able to induce crown-gall tumors on plants with strains of *Agrobacterium rubi*, the so-called "cane-gall organism." Klein and Klein (1953) showed that *A. rubi* could be transformed into a "crown-gall organism" by the desoxyribonucleic acid of a crown-gall strain. They concluded that the ability of any particular strain of bacteria to induce tumor formation in any particular host is conditioned by the presence in the bacterium of hereditary factors that control its production of tumor-inducing agents effective in that host. The presence, in any strain or "species" of the bacteria, of the hereditary factors controlling virulence for one host did not prevent the acquisition of factors controlling virulence for another host. Host specificity would appear to involve a genetically controlled production of structurally or biologically specific tumor-inducing agents. As will be shown below, it is unlikely that the inability of cells of a particular host to become tumorous is primarily a reflection of the inability of the bacteria to produce the agents active in that host (cf. McKeen, 1954b).

There is a wide range in the disposition of different strains of virulent crown-gall bacteria to bring about tumor-cell formation. Some strains are highly virulent, as measured by the growth rates and eventual sizes of the resulting tumor. Others are intermediate in virulence, and some are almost avirulent in that they incite only formation of very small, slow-growing tumors. Strains also have been isolated which regularly induce the formation of tumors with characteristic gross and microscopic morphologies. The effects of these types of bacteria and the study of their resulting tumors will be examined later.

In this and other sections of the review, many of the etiological factors which delimit the range of reactability of the cells under consideration are examined in detail. At the present time, it is only possible to conjecture to what extent the reported findings specifically may be related to alterations of a normal cell into a primary tumor cell. If induction is a necessary part of the complex of primary transformation, then the formation of a primary tumor cell requires that induction take place and that susceptible cells be available for induction. But failure of a tumor to appear does

not prove that induction did not take place. There are several factors which, to date, have not been shown to bear a specific relationship to any particular transformation process or event, although they may be limiting factors in tumor-cell initiation and development. With these precautions in mind, the following findings on the interrelations of host and bacteria are of interest.

Montimartini (1938) and Elliott (1951) have compiled lists of the plant species that are susceptible or resistant to tumor formation following their inoculation with known strains of crown-gall bacteria. These lists are not as definitive as might be expected, since many of the plants may form tumors if inoculated with different strains active for those plants (cf. Kauffmann, 1928). With rare exceptions (cf. DeRopp, 1951c), it was found that no monocot is truly susceptible, but that at least one member of almost all classes of dicots can form tumors if inoculated with one or another of the strains of bacteria. Klein (unpub.) assumed that the failure of monocots to form tumors may have been due to the absence of a true cambium. He has tested, with negative results, species of monocots whose steles show some type of cambium (*Yucca*, *Dracena*, etc.). DeRopp (1950) has reported that carrots of the same variety may form large tumors, tumors of varying but moderate size, or no tumors at all. No adequate explanation has been published to date to account for these findings.

Smith and Quirk (1926) reported that crown-gall bacteria cannot grow at pH values below 5.7 and that a *Begonia* with a sap at pH 1.5 did not form tumors upon inoculation. Yet other plants which have quite acid saps are capable of initiating tumors. Hornbostel (1939) found that the crown-gall bacteria may be inactivated in vitro by the acid saps of several plants that were susceptible to tumor formation. Rybak (1946) and Hayes (1946) have shown that a number of plants contain sap that inhibited the growth of crown-gall bacteria but that many of these plants were very susceptible to tumor formation when inoculated with the same strains of the bacteria.

Many workers have observed that the age and vigor of the host are important factors in tumor initiation. Friedemann and Magnus (1915), Blumenthal and Hirschfeld (1917), Levine (1921b), and Berthelot and Amoureux (1938a) found that plants which showed the best vegetative development showed maximal tumor development. Berthelot and Amoureux (1936a), Appler (1951), and Rack (1953) found that young plants were more susceptible than older ones. Stapp and Bortels (1931) and Klein (1952) reported that only vigorous tomato plants were fully susceptible, a finding also applicable to apple (Riker and Hildebrand, 1934). Link, Wilcox, and Link (1937) and Link et al. (1953) reported that nitrogen-deficient plants sometimes fail to form tumors in their older internodes although upper (younger) internodes of the same plant invariably initiated tumors following inoculation. Price and Gainor (1954) found that removal of terminal leaves reduced tumor size. Appler (1951) could not induce tumors on decapitated stems of old sunflower plants. Magnus (1918) has observed polarity differences and position effects on carrot which affect the ability of the tissues to form tumors. It has been shown that neither white light (DeRopp, 1948c) nor light passed through red or green filters (Flint and Moreland, 1945) has any effect on tumor initiation in spite of the well-known effects of visible radiation on normal morphogenesis. Many workers (cf. Riker and Berge, 1935) have observed that a single strain of crown-gall bacteria will induce morphologically distinct tumors on different hosts. Thus, in the genus *Nicotiana*, a single strain of bacteria induced hard, short-lived tumors on *N. langsdorffii* and large, soft, long-lived tumors on *N. glauca*.

A considerable body of information is available on the phenomenon of immunity of plants to tumor genesis. Riker and Berge (1935), Magrou (1935, 1948), Savelescu (1936), and Gäumann (1948) have reviewed much of the information pertaining to this subject. A number of investigators have reported that extracts of tumors from many hosts were capable of agglutinating or precipitating *Agrobacterium tumefaciens* in vitro at greater dilutions than similar extracts of normal tissue (Berridge, 1929; Magrou, 1935, 1938; Magrou and Lominski, 1937). Schiff-Giorgoni (1905) noted the presence of a thermolabile, antibacterial substance in tumors on olive trees, but Korinek (1924) stated that this and similar substances were "pseudo-agglutinins" and demonstrated that they were not specific for tumor-inducing bacteria. Other investigators failed to find any agglutinins in tumor tissues (Riker, 1926; Lasseur and Renaux, 1935). Rybak (1948, 1949) has begun a series of critical studies on this subject with some highly significant results. He has reported that the agglutination of bacteria by extracts of tumors is due to the presence of large amounts of tannin and tannic acid in the tumor (cf. Manigault, 1953). These tannic acids have been shown to act as agglutinins. Rybak (1948)

also reported that a feeble bacteriophage was occasionally present in tumors of geranium, and this could agglutinate but not lyse the bacteria. It is possible that this is a lysogenic bacteriophage. It was shown that this 'phage was specific against crown-gall bacteria.

Several authors have observed that the presence of one tumor on a plant will prevent the formation of another tumor if the "super-infection" was made within a few centimeters of the growing tumor (Manil and Straszewski, 1949). Arnaudi (1925, 1928) and Duyfjes (1935) reported that plants were less susceptible to tumor formation if the plant already bore a tumor. Tumors formed following the second inoculation usually remained smaller than the first tumor. Magrou (1935, 1938) reinoculated tumor-bearing geranium plants in the internodes above and below the growing tumor and noted that the new tumors grew slowly, if at all. Gäumann (1948) termed this type of reaction "humoral pre-immunity," indicating that immune bodies are produced in the host in the presence of the tumor and are capable of diffusing into presumably healthy tissues. Straszewski and Manil (1952b) found that when *Datura* plants received multiple punctures at the same time all the tumors grew at the same rate, but if three weeks elapsed between inoculations, the second inoculation resulted in small, slow-growing tumors. These findings have not been confirmed by other workers. Brown (1923), Redealli (1934), Nobecourt (1928), and Riker and Berge (1935) have presented data showing no protection of plants by previous inoculations. Rybak (1947, 1953) has reported that the resistance of geranium to a second inoculation is due to the presence of small molecules formed in the tumor which can diffuse into adjacent, nontumerous tissues. The globulin fractions of either tumorous or normal were inactive, and he concluded that the immunity was not analogous to animal resistance.

"Acquired immunity" in crown-gall (Gäumann, 1948) also has been reported. Gheorghiu (1932) found that a bactrin (a suspension of heat-killed cells) of *Agrobacterium tumefaciens* would protect geranium plants for up to three months following its injection into the stems. Carbone and Arnaudi (1930) prepared an antiserum in rabbits inoculated with crown-gall bacteria and placed geranium stems in this serum. When the plants were subsequently inoculated, tumors did not develop and preformed tumors dried up within two weeks. Straszewski and Manil (1952a) filter-sterilized liquid cultures of crown-gall bacteria and injected this filtrate into *Datura* plants. The plants were inoculated four days later, and the subsequent course of tumor development was followed by measuring the size of the tumor masses. Fewer tumors were formed on the "sensitized" plants, and those which appeared remained quite small. When this filtrate was supplied through the roots prior to inoculation, the appearance of tumors was delayed and these developed slowly. In contrast to the report of Gheorghiu (1932), Straszewski and Manil (1952a) were unable to observe any protection with bactrin preparations.

It is impossible at the present time to state categorically that immune states exist, or do not exist, in plants. The positive experiments reviewed above are generally unsatisfactory because of the failure to observe proper control techniques. Water, for example, is not a control for serum, and sterile uninoculated medium is not a control for a filtrate of a virulent bacterial culture. Preinoculation, with attendant modification of the host as a result of tumor metabolism, does not adequately control studies on second inoculations. The lack of a closed circulatory system and the absence of intercellular proteins in plants would indicate that if immunity states do exist, they are different in kind than those in animals.

The first experiments which laid the basis for the eventual demonstration that specific etiological agents are active during the Induction Phase of tumor-cell genesis were done by Riker (1926a). He reported that at air temperatures above 30°C., tumors did not form following inoculation with virulent bacteria, although host, pathogen, and previously formed tumors all grew well at or even above this temperature. At 27°C., or below, good tumors were formed; above 28°C., the tumors were small. In tobacco, some tumors were formed at 32°C., but these remained quite small and were not macroscopically evident until about ten days later than those induced at 26°C. (Riker, Lyneis, and Locke, 1941). Riker et al. suggested that their findings might indicate some unknown change in the host-parasite relationship at elevated temperatures, a change which could be correlated with pathogenicity.

The great importance of these findings was recognized later by Braun (1947a). He confirmed the earlier reports of Riker that 32°C. did not interfere with the growth of the host, with wound-healing, or with the multiplication of the bacteria in situ. There was no inhibition of the growth of the

tumor above 32°C., once primary tumor cells had been formed. Other experiments demonstrated that the effect of the elevated temperature is not on the susceptibility of the whole plant but that the temperature effect is restricted to the immediate site of bacteria-host contact. By inoculating *Vinca* plants held at 26°C. and then transferring some of them to 32°C., at various time intervals, he found that Transformation could be accomplished only during the 4-day period following inoculation. Braun also found that there was a lag of somewhat more than one day between the time of inoculation and the time of tumor-cell induction. It was during the second to third day that temperatures above 30°C. inhibited induction. These results were confirmed by Segretain (1949) and others.

In 1947, Braun (1947a) reviewed his work on tumor induction in its relationship to time and temperature and suggested that a substance which is responsible for cellular alteration and which he termed a "transformation principle" or "tumor-inducing principle," is either heat-labile at 32°C. or is rendered inactive by some cellular constituent at this temperature. This agent, the tumor-producing principle, will hereafter be designated by the abbreviation "TIP."

To test these hypotheses, Braun and Mandle (1948) conducted a series of experiments on *Bryophyllum* plants. They found that the minimum time required for transformation at 25°C. was about 32 to 36 hours after inoculation. When the plants were conditioned for one day at 32°C., a subsequent exposure of inoculated stems to 25°C. for 10 to 14 hours was sufficient to permit some cellular alteration. Large, rapidly growing tumors were, however, induced within about 48 hours at 25°C., following conditioning. These results indicated that TIP is either heat-labile or is not formed at 32°C. To gain more information on this point, Braun and Mandle (1948) studied the cumulative effects of TIP. All plants were conditioned for 24 hours at 32°C. following their inoculation. Plants were then intermittently maintained at 25°C. for 30 hours, alternating for 7½- or for 6-hour periods with 1- to 6-hour intervals at 32°C. The results clearly indicated that the effective titer of TIP was cumulative. As the total time at 32°C. increased relative to the total time at 25°C., the size of the resulting tumors decreased. When the time at 25°C. exceeded the time at 32°C. by less than 10 hours, no tumors were formed. Thus, the biologically active titer of TIP could be computed on an "hour-unit" basis. Assuming that ten hour-units of TIP are necessary for minimal transformation, an excess of 10 hours at 25°C. over the time at 32°C. would be required. Eighteen to twenty-four hour-units of TIP appeared to be necessary for optimal tumor-cell induction. It would appear that TIP was destroyed at 32°C. at about the same rate that it was formed at 25°C. (cf. Klein, 1953).

Determination of the chemical nature of TIP is an important challenge to students of crown-gall. By precise temperature control studies, Braun (1950) showed that the lower limit of inactivation or destruction of TIP lies in a temperature range of less than two degrees. The activation energy for the destruction was computed according to the Arrhenius coefficient and found to be of the order of 80,000 calories per mole. Since protein denaturation reactions are of this order, Braun suggested that TIP, or something intimately associated with its inactivation, may be "a factor of complex structure." Some recent findings by Klein (1952) also bear on the nature of TIP. He observed a peak in the concentration of desoxyribonucleic acid (DNA) in tomato tissues within 24 to 48 hours after inoculation with crown-gall bacteria. Subsequent work (Klein, Rasch, and Swift, 1953; Klein, 1953) showed that this high DNA peak was not related to changes in number of host cells, presence of the bacteria in the tissues of the host, or to the amount of DNA in the host cells as determined by quantitative cytochemical methods. Histochemical examination of the affected cells showed no evidence of this DNA in either the nuclei or the cytoplasm, indicating that it is probably different in nature from the DNA present in tissues and cells of higher plants. These differences may be structural or may be due to a lower order of polymerization. There are indications that both distinguishing characteristics may be involved.

Later, Klein (1953) found, in tissues of tomato stems inoculated with (1) fully virulent, (2) attenuated, or (3) avirulent bacteria altered into virulent forms (Klein and Klein, 1953), that the level of DNA increased to 200 per cent of control values within 24 hours, remained at this high level for an additional 24 hours, and then decreased to control levels by 72 hours after inoculation. Tissues inoculated with unaltered avirulent bacteria showed no increase in the level of DNA. When the plants were held at 30°C. for a 3-day period following inoculation with virulent bacteria, the observed DNA level was less than half that at

25°C., and the curve broke sharply within 48 hours. This result suggests a heat-induced depolymerization of the DNA.

On the assumption that TIP is a specific polymer of DNA, several facts may be fitted into a rational pattern. The time of the appearance and disappearance of the DNA peak is the same as the biologically observed time of the activity of TIP (Braun, 1947a). The absence of a DNA peak in tissues inoculated with a completely avirulent strain of crown-gall bacteria and the occurrence of this peak in tissues inoculated with the same strain of avirulent bacteria which had been altered into moderately virulent bacteria (Klein and Klein, 1953) also fit this hypothesis. The apparent low rate of DNA synthesis (representing a net excess of synthesis over destruction) at 30°C. corresponds to the known heat-lability of TIP (Braun and Mandle, 1948). The finding that attenuated strains of bacteria (Van Lanen, Baldwin, and Riker, 1940, 1952), which require only the addition of auxin in order to complete transformation of normal into primary tumor cells, also induce the DNA peak in inoculated tissue, is not incompatible with this hypothesis. Finally, polymerized DNA meets the requirements for "a factor of complex structure" (Braun, 1950). Nevertheless, the final identification of TIP as being a specific polymer of DNA must wait until this DNA is isolated, characterized chemically, and tested biologically for its ability to induce tumor-cell formation.

Data bearing on the source of TIP are valuable in determining its nature and its action on conditioned cells, as well as in contributing to our knowledge of its etiological role. Several lines of evidence indicate that it is a metabolic product of both virulent and attenuated crown-gall bacteria. Waksman et al. (1944), DeRopp (1949a), Dye and Hutchinson (1950), and Colasito et al. (1951) found that several antibiotics, aureomycin, penicillin G, streptomycin, etc., were antibacterial for crown-gall bacteria. Ark (1947) failed to inhibit the bacteria in vitro with streptomycin, but it appears that his effective concentrations were too low (Dye, pers. commun., 1953). DeRopp (1948c, 1949a, 1954) has conducted a series of experiments on the effects of antibiotics on tumor induction. When carrot cylinders were transferred to media containing streptomycin within 48 hours after inoculation, only a low percentage of the cylinders formed even small tumors. If six or more days elapsed between inoculation and treatment, all the cylinders formed large tumors. No significant regression or inhibition of the growth of the tumor tissue was observed with the concentrations used. Tumor formation was evident if streptomycin-resistant strains of crown-gall bacteria were used. Aureomycin, terramycin, and chloroamphenicol were capable of inhibiting the bacteria in vitro but did not prevent tumor formation. DeRopp (1954) indicated that bacteriostasis may not always accompany loss of tumor-inducing ability, but no experiments were reported which tested the effectiveness of the antibiotic in plant tissues. Blanchard (1951) extended these findings to tomato plants grown in nutrient solutions containing aureomycin (cf. also Rybak, 1947; Manigault, 1953). Dye and coworkers (1950, 1951, 1952), using crude and commercial antibiotics in relatively low concentrations, repeated these studies. The time relations of inhibition of tumor-cell formation by bacteriostasis suggest that the TIP synthesis was inhibited as a consequence of the inhibition of the growth and metabolism of the bacteria. Additional support for the hypothesis that TIP is formed by the bacteria is found in reports dealing with lysis of the bacteria (Kent, 1937). Bacteriophage treatments of cultures of crown-gall bacteria destroyed their ability to induce tumor formation.

Another line of evidence favoring the hypothesis that TIP is synthesized by the bacteria has recently been presented by Klein and Klein (1953). They showed that completely avirulent strains of crown-gall bacteria (and avirulent species of related bacteria) could acquire the property of virulence by culture in media containing DNA isolated from virulent crown-gall bacteria. Coleman and Reid (1949) previously made somewhat similar observations. Virulence, once acquired, appeared to be genetically fixed, indicating that a hereditary unit for virulence had been acquired by bacteria which initially were deficient for that unit (cf. Ephrussi-Taylor, 1951; Lederberg, 1952). The synthesis of TIP by the bacteria appears, therefore, to be a function of the presence and activity of hereditary units regulating the production of TIP. Avirulent forms did not induce a DNA peak in inoculated tissues, but those bacteria altered by transformation reactions into virulent bacteria and carrying the acquired hereditary potential for TIP synthesis did evoke this DNA peak (Klein, 1953).

Although the available information strongly suggests that TIP is a metabolic product of crown-gall bacteria, the bacteria apparently do not syn-

thesize it in the usual laboratory media. Many attempts have been made to induce crown-gall tumor formation in plants with media in which virulent bacteria had been grown or with fractions of the bacteria. Kauffmann (1930), Brown and Gardner (1936, 1937), Chargaff and Levine (1936), Link, Wilcox, and Link (1937), Levine and Chargaff (1937), Manil and Straszewski (1951), and Klein and Klein (1953) all have reported negative results. These failures indicate that the synthesis of TIP occurs only under special conditions found in plant tissues. Preliminary studies (Klein and Knupp, unpub.) have now shown that these conditions may include suitable concentrations of wound substances. When virulent bacteria were grown in synthetic medium containing extracts of wounded tomato tissues, the bacteria-free medium was capable of inducing the formation of crown-gall tumors which were sterile and capable of unlimited growth when grafted into healthy plants. The finding that heat or protamine sulfate (a nucleic acid precipitant) inactivated the medium may be a further indication of the nucleic acid nature of TIP.

Here, then, in the Induction Phase, is a second etiological role for wound substances in addition to their role in the conditioning phase. Wound substances apparently are required not only for the conditioning of prospective tumor cells but may also be necessary for the synthesis of TIP by the bacteria. Wound sap may supply either the necessary precursors for TIP synthesis, cofactors for this synthesis, or substances shunting the synthetic metabolism of the bacteria into TIP synthesis. Once wound-healing starts, the supply of these substances to the bacteria probably becomes restricted not only by the formation of mechanical barriers, but also by their utilization within the host cells for their own metabolic activities.

It would be appropriate at this point to speculate on the possible modes of action of TIP. This, however, is deferred in order to present in proper sequence the data bearing on other etiological factors and to examine certain other studies pertinent to the problem of the role of TIP in tumor-cell formation.

A few studies bear on the effects of TIP and other etiological factors and agents on the structure or the functional behavior of the incipient tumor cell which has experienced induction. No evidence of cell division or of cell enlargement other than that due to wound response can be seen 48 hours after wounding and inoculation of tomato plants (Riker, 1923b; Klein, 1952; Klein, and Link, unpub.). In the broad bean, however, limited cell activity was noted in vascular-associated parenchyma by this time (Rasch, unpub.). Link and Goddard (1951) reported an increase in the oxygen uptake of inoculated tissues within 48 hours, but Klein (1952) found decreased rates of oxygen uptake at this time. There was a significant increase in the fermentative ability of slices of inoculated tomato stem tissues taken from the wounded areas, an increase not noted in uninoculated wounded tissues. There were slight increases in protein and soluble nitrogen. Acid-soluble organic phosphorus compounds were also slightly increased. Link and Eggers (unpub.) have found an increase in the auxin concentrations of the inoculated tissues.

Prior to the development of the concept of TIP as the second major agent active in transformation of a normal cell into a tumor cell, a number of substances, many of them complexes of biological origin, were tested as possible "causes" of the tumorous change. Smith et al. (1911) were probably the first to suggest that the bacteria act by the production of specific "toxins." Boivin et al. (1935) reported that an endotoxin prepared from crown-gall bacteria induced tumor formation in geranium. No confirmation of this report has appeared (Gheorghiu, 1938; Feder and Ark, 1951; Demetriades, 1953). Riker and Berge (1935) have cited over fifty examples of compounds which induce some proliferation in plant tissues. In other reviews (White, 1950; DeRopp, 1951c) some attention was paid to those reports which evaluate the effects of temperature, moisture, light, etc., on the production of neoplasms. In no case were the overgrowths induced by the tested chemical, nor those incited by environmental conditions, identical with crown-gall tumors; and none of the inciting substances showed the known characteristics of TIP. Levine (1936) and DeRopp (1951c) have reviewed at length the studies dealing with the application of carcinogenic and mutagenic agents. Although the resulting neoplasms were, in some cases, morphologically similar to crown-gall tumors, they were neither autonomous nor physiologically comparable to crown-gall tumors. It may be concluded that crown-gall induction processes are unique in that, in the affected cells, a special set of circumstances and particular etiological factors and

agents are operating. Other types of neoplastic responses in plants are, however, within the adaptation range of the cells.

To summarize the possible course of events in the Induction Phase: the main etiological agent active at this time seems to be a metabolic product of the bacteria. This agent—the tumor-inducing principle—is synthesized by those strains of bacteria which possess or have acquired the proper hereditary constitution. The tumor-inducing principle may be a special polymer of desoxyribonucleic acid that is synthesized only in a milieu of wound sap. It acts on conditioned cells during the 10- to 24-hour period following the conditioning phase. Cells which in addition to conditioning also have received the stimuli provided by the tumor-inducing principle, are here designated *incipient tumor cells*. An incipient tumor cell may be considered to have acquired the potential for tumorous growth and development and is positively predisposed to the action of those other etiological factors and agents which are essential to transform it into a primary tumor cell. The incipient tumor cells are not characterized by any special histological or cytological modification nor by well-marked physiological alterations. There is some presumptive evidence that they may be metabolically more active than their normal counterparts.

Promotion and Completion Phase

Braun and Laskaris (1942) advanced the proposition that induction is the last stage in the change of a normal into a tumor cell and that subsequent changes in the tumor cell and its progeny are aspects of stimulation of a tumor cell to a more than normal rate and frequency of cell division, so as to produce either small or large tumors, depending upon the amount of cell division.

In this review the Transformation Period is considered to include those alterations in an incipient tumor cell which promote and complete its change into a primary tumor cell. If Braun's proposition proves the valid one, then the changes here considered to belong to the Promotion and Completion Phase of the Transformation Period, belong within the period herein designated as the Duplication Period.

Nemec (1930) assumed that cultures of *Agrobacterium tumefaciens* smeared on cut surfaces of the root of *Chichorium intybus* produced a growth substance which was responsible for the callus growth, enhanced initiation of adventitious roots, and suppressed development of adventitious buds which he noted in the treated root. Solacula and Constantinesco (1936) reported that, upon adding indoleacetic acid (IAA) to sterile Knop's solution containing sterile decotyledonized seedlings of *Phaseolus* or *Ricinus communis*, they obtained gross inhibitory or stimulatory effects in these plants, in accordance with the concentration of the acid. Tumor production was one of the observed effects. They noted that both excessive cell enlargement and division, as well as disorientation of meristems, occurred in the treated plants. Removal of the affected plants to Knop's solution free of IAA was followed by resumption of normal growth. Brown and Gardner (1936) reported that ether extracts of cultures of *Agrobacterium tumefaciens*, when applied in agar to decapitated internodes of bean and other plants, led to tumor formation which in appearance and behavior simulated crown-gall tumors. They also found that application of IAA in lanolin had the same effect and pointed out that their findings might have some bearing on the search for chemical entities whereby the bacterium produces crown-galls.

Link, Wilcox, and Link (1937) and Link and Wilcox (1937) applied ether extracts of the pellicles of cultures of *A. tumefaciens*, the culture medium in which the bacteria had been grown, or the tumors of crown-gall, in each case mixed into lanolin, to intact hypocotyls of bean and tomato, and obtained neoplastic swellings. They showed, by the Salkowski test, that these extracts, as well as those of other tumor-inducing bacteria, fungi, or insects, probably contained IAA. They tested the effects of various concentrations of IAA in lanolin upon all vegetative organs of the red kidney-bean and of some of the organs of the tomato plant, and studied the wound responses of these organs to sterile wounds of various severity. Lethal, inhibitory or stimulatory gross effects, including retardation of straightening of the arch of the bean seedling, and tumor formation could be produced, depending on the concentration of IAA used, the kind of plant tested, the organ of the plant tested, and the age and stage of development of the organ.

Berthelot and Amoureux (1938) demonstrated the presence of IAA in liquid media containing tryptophan in which crown-gall bacteria had grown. No IAA was found in the absence of tryptophan. They concluded that "it appears probable that indoleacetic acid plays an important role in

crown-gall production." Dame (1938) found that the synthesis of IAA by crown-gall bacteria was stimulated by tryptophan in the media, although virulent cultures produced IAA even in the absence of this precursor. Non-virulent ("attenuated") strains, however, did not produce IAA at all in the absence of tryptophan, and only small amounts even in its presence. Gioelli (1940) found that synthetic IAA, as well as extracts of the culture fluids of virulent bacteria, were capable of inducing neoplasms in plants and also concluded that IAA was a metabolic product of crown-gall bacteria.

Histological examination of the auxin-induced tumors of bean and tomato plants showed essentially the same changes which had been reported for the bean by Kraus, Brown, and Hamner (1936) after decapitation of the second internode and application of IAA in lanolin. The cellular changes noted were excessive cell enlargement and division, deficient differentiation, and excessive local differentiation in the form of vascular-like elements and vascular bundles and adventitious roots. All new tissues formed were pathologic, in that they did not have the survival value of normal tissues, either drying out or rotting prematurely.

Finally, Link, Wilcox, and Link (1937) pointed out that though growth substances supplied by the bacteria might play roles in tumor production, they could not be considered as constituting more than one factor or agent in a causal complex in which each constituent is a *necessary*, but not a *sufficient* cause, and that heteroauxin (IAA) is "a chemical agent by means of which possibly, in conjunction with others, *P. tumefaciens* incites galls."

In order to prove the necessity of auxins in the genesis of tumor cells and tumors, it was necessary to find crown-gall bacteria which do not bring about more than a minimal primary transformation (or, according to Braun's proposition, more than minimal stimulation of tumor cells to abnormal rates and frequencies of division) and to determine whether supplied growth substances can specifically be used as etiological agents effecting superminimal transformation (or stimulation).

The ability of different strains of the crown-gall bacteria to induce tumors had been examined by many workers. Fully virulent cultures were found to retain their ability to induce tumors for many years (Levine, 1936), even on a completely synthetic medium (Riker, 1942). Of special interest were strains incapable of inducing superminimal tumor-cell transformation or optimal tumor growth. Many of these strains are completely avirulent. These may be presumed to lack the ability to synthesize TIP (Klein, 1953). Other cultures, obtained as single cells isolated from populations of virulent cells (Hendrickson, Riker, and Baldwin, 1934) and unable to induce good tumor growth, may be presumed to synthesize TIP (Klein, 1953). These have been designated "attenuated" crown-gall bacteria. In some trials, and with some hosts, very small slow-growing tumors have been produced with these bacteria, while other inoculations have not resulted even in the formation of detectable tumors. The demonstration that attenuated cultures did not complete tumor formation or produced only small tumors prompted a search for substances which could replace the lost ability of the attenuated inoculum to effect more than minimal transformation (or to bring about superminimal stimulation of the tumor cell).

In a series of experiments Riker and his associates (1936–1941) investigated the relations of growth substances, and of indoleacetic acid in particular, to crown-gall production. They used a virulent and an attenuated strain of *A. tumefaciens* and the nonvirulent *A. radiobacter* as test bacteria. In their first two papers Locke, Riker, and Duggar (1937, 1938) reported that inoculation of various plants with cultures of the virulent and attenuated strains produced differential effects, including tumor production in various hosts, organs, and tissues. In addition to producing large tumors, the virulent strain brought about epinasty, enhanced the production of adventitious roots and cambial activity, delayed abscission of leaves, and inhibited adventitious bud development. The attenuated strain, on the other hand, produced small or no tumors, but did induce epinasty as well marked as that produced by the virulent strain, enhanced adventitious bud formation and delayed the abscission of leaves. It did not affect cambial activity so far as production of secondary xylem was concerned, nor the development of adventitious roots. Locke, Riker, and Duggar concluded from their findings that growth substances are associated with crown-gall tissues and are a limiting factor in the development of galls when the attenuated strain is used for inoculation.

By means of the *Avena* coleoptile technique they also tested ether extracts of cultures of the virulent and the attenuated strains of *A. tumefaciens* and of the nonvirulent *A. radiobacter* for their auxinic

activities. They found that the first two extracts were equally effective and about four times as strong as those of the nonvirulent *A. radiobacter*.

To determine whether failure of the attenuated strain to produce large tumors in tomato was associated with the absence of growth substances, they inoculated the attenuated strain into plants and then inoculated the virulent strain at loci above the first site of inoculation. Following this treatment the lower inoculation produced large tumors. They also inoculated the attenuated strain into plants, decapitated some of these, and found that the tumors were larger in the intact plants than in the decapitated. The bacteria isolated from the "attenuated" tumor still were attenuated. They concluded that some substance that diffused from the top of the intact plant or from the gall produced by the virulent culture stimulates the attenuated strain to produce large tumors. Finally, to test whether this diffusing substance might be indoleacetic acid, they inoculated plants with the attenuated strain, decapitated them, and then applied IAA in lanolin paste to the wound surface. They reported a slight stimulation in tumor growth, but less than that noted in intact plants or in plants also inoculated with the virulent strain above the site of the inoculation with the attenuated strain.

In a third paper Locke, Riker, and Duggar (1939) gave consideration to "the possibility that the cause of pathogenicity, as suggested, for example by Nemec, Brown and Gardner, Link et al., and as claimed by Berthelot and Amoureux" is indoleacetic acid produced by the bacteria. They accordingly repeated and extended their previous study of the auxinic activities of extracts of a virulent and an attenuated strain of *A. tumefaciens* and of the nonvirulent *A. radiobacter* grown on peptone-tryptophan media. They found that although the attenuated strain produced less auxin than the virulent one, no significant differences occurred, and they concluded that "while the possibility still remains that the formation of growth substances by the crown-gall organism from the materials available to it within host tissues may constitute a part of the mechanism leading to excessive growth . . . the evidence seems lacking that beta indoleacetic acid or any other known growth substance produced in such cultures has a direct major relation to the pathogenicity of crown-gall bacteria."

After Lefebre (1938) demonstrated that IAA occurs in green plants, Locke, Riker, and Duggar (1939) set out to determine whether the growth substance occurring in a crown-gall affected plant is different from that produced in culture by the bacteria, and whether the growth substance in the gall is produced by the bacteria in the host. They used the techniques devised by Kögl and his associates (v. Audus, 1953) to distinguish auxins of the a and b types and of heteroauxin (IAA). On the basis of their findings, they concluded that the growth substance in the gall and host are similar and resembled IAA. They again concluded "to reserve judgment about indoleacetic acid being the major cause of gall formation" because the amount of growth substance detected in crown-gall was a very small fraction of that required to produce similar proliferation with artificial application; because substances diffusing from inoculation with virulent strains stimulated gall development following inoculation with the attenuated strain while even strong applications of IAA did not; and because responses of a number of plants inoculated with the organism failed to parallel their reactions to applications of indoleacetic acid.

Riker, Henry, and Duggar prepared ether extracts and agar diffusates from inoculated and non-inoculated stems of (1) intact tomato plants 1, 4, 8, and 16 days after inoculation; (2) decapitated and intact inoculated and noninoculated plants; and (3) inoculated plants, kept at 27°C., which produce galls, and at 31°C., which do not. They then determined the auxinic activity of these extracts by the *Avena* coleoptile test. They considered total nitrogen content of the extracted tissues a better base than either their wet or dry weights, for calculating the values of the auxinic activities. They found no statistically significant differences in tests between the auxinic activity of extracts of control and inoculated intact plants. Galls from decapitated plants were smaller than those of intact plants, and their extracts had auxin activities about one-half as much as those of the latter group. The auxinic activities of extracts of inoculated plants, whether kept at 27°C. or at 31°C., were the same. Riker, Henry, and Duggar reported that while they confirmed the experimental results of other investigators and produced more evidence shedding light upon the interpretations of these results, the interpretations needed revision; and they concluded that there was "no satisfactory evidence showing that the pathogenicity of crown-gall bacteria can be attributed to the production of IAA or similar growth substances measured by the techniques here employed." They then tested other substances produced by *A. tumefaciens*, such as

thiamin, etc., and concluded from those tests that there was no proof that any of these substances are related to tumor induction singly, but that they might "be active in association."

Link and Eggers (1941) reported results of extensive determinations of the auxinic activity of extracts in water, ether, or both, of fresh and lyophilized samples of control and inoculated hypocotyls of tomato. In every test the extracts of the inoculated tissues were auxinically more active than those of the control. The results indicate that the inoculated tissues yielded both more "free" and "bound" auxins than did the controls (Gordon, 1953, 1954).

Braun and Laskaris (1942) observed that the degree of cellular alteration at the site of inoculation of attenuated bacteria was roughly comparable to that found in early stages of transformations induced by virulent bacteria. They repeated the experiments of Locke et al. (1938) with attenuated bacteria, applying IAA, naphthaleneacetic acid (NAA), and indolebutyric acid to decapitated stems of inoculated plants. In contrast to Locke's results, Braun and Laskaris obtained voluminous tumors within a few weeks. Indolebutyric acid was the most effective in the tests, followed by IAA and NAA. They were unable to observe any increase in the virulence of the bacteria, the isolated bacteria still being attenuated. The resulting tumors could be transplanted into healthy plants where they proliferated as true tumors, in contrast with auxin-induced neoplastic tissues which will not grow as graft transplants. This was a convincing demonstration that the tumors resulting from the combined action of the bacteria and of the auxin were true crown-gall tumors. Braun and Laskaris concluded that a hormonal effect was a necessary, but not sufficient, factor for tumor-cell formation. Thomas and Riker (1943, 1947, 1948), using a number of synthetic growth regulators, extended these results to other plants. It is significant that synthetic auxins were more effective than natural auxins in causing the formation of tumors. This finding of Thomas and Riker, together with the report of Braun and Laskaris, suggests that natural auxins may be rapidly oxidized by the host tissues, reducing their concentration at the site of action below an effective level. It may be concluded that a normal cell which has been altered by conditioning processes and by the subsequent action of TIP, will not be completely transformed, in the absence of growth substances, into primary tumor cells which will produce a large tumor.

Two questions arose out of the work of Braun and Laskaris: (1) what are the temporal relations between the actions of TIP and auxin? and (2) how long may an incipient tumor cell remain positively predisposed to the co-carcinogenic or promoting action of auxin? Following the experimental procedures of Braun and Laskaris, and using a synthetic auxin to minimize auxin destruction in vivo, Klein and Link (1952) demonstrated that auxin was inactive as a promoting agent before the end of the Induction Phase (about 36 hours after the inoculation of attenuated bacteria). The removal of the auxin prior to this time completely prevented the formation of tumors. From 36 to about 72 hours after inoculation and the application of auxin the size of the resulting tumors was proportional to the length of the "auxin presentation time." After the 72-hour period, there was no further need for supplementary growth substances. These results showed that both a high titer of growth substance and a definite presentation time are required for optimal promotion of the TIP-altered cells.

Klein and Link (1952) accordingly considered the growth substance a co-carcinogen or a tumor-promoting agent necessary for promotion of an incipient tumor cell into a primary tumor cell. [Braun (1942) takes it to be an agent which stimulates a tumor cell to divide. According to his interpretation, the failure of attenuated strains to incite formation of large tumors is not due to a lack of capacity to induce tumor cells, but to failure of the bacteria to stimulate the tumor to divide.]

The answer to the second question was not so definite. By withholding auxin for various lengths of time after inoculation with attenuated bacteria, it was found that when 15 or more days elapsed between inoculations and the start of auxin treatments, the resulting tumors contained root primordia. This suggested that the host plant had, to some extent, regained control over the development of the tumorous tissues. Braun (pers. commun.) has shown that tumors will develop as long as six weeks after inoculation with attenuated bacteria when a virulent culture is inoculated above the attenuated culture. This indicates that incipient tumor cells may remain predisposed to promotion (or to stimulation) for at least six weeks. It is probable that the growth substances of rapidly growing tumors are more selective promoting agents than the synthetic substances and may have fewer side effects.

Straszewski and Manil (1950) reported that a

heavy suspension of their strain of crown-gall bacteria would induce tumor formation, although a diluted inoculum required additional IAA for satisfactory tumor formation. One suspects that their bacteria may have been partially attenuated. If this is true, their findings would tend to support the conclusions of Braun and Laskaris (1942) and of Klein and Link (1952).

It has been found that crown-gall bacteria may be attenuated by chemical treatment. Van Lanen, Baldwin, and Riker (1940) reported that 10 to 20 serial transfers on a medium containing glycine attenuated the bacteria. It is impossible at the present time to determine whether this attenuation represents a selection of attenuated bacteria existing in a population of virulent bacteria or whether it is an instance of a directed mutation. Compounds possessing a glycine configuration (alanine, leucine, etc.) were as effective as glycine. Longley et al. (1937) found that strains of legume root-nodule bacteria (*Rhizobium*) could be similarly attenuated, glycine-treated cultures failing to induce root nodule formation on susceptible plants. These preliminary studies were extended by Van Lanen and coworkers (1952), who demonstrated that there were only slight modifications in the growth behavior and enzyme activity of attenuated strains. Riker and coworkers (Riker and Berge, 1935) have examined the growth behavior of one or more of the attenuated cultures in experiments run in parallel with virulent cultures. Many aspects of the growth, metabolism, and biochemical behavior of these strains were examined, and it was clear that, in general, their physiology was not very different from that of virulent bacteria.

Complete virulence and non-dependence of the bacteria on extrinsically supplied auxin for optimal tumor formation could sometimes be restored to glycine-attenuated bacteria when they were serially transferred on glycine-free media. The degree of reactivation was inversely proportional to the number of passages on the glycine medium and was directly proportional to the subsequent number of glycine-free subcultures (Van Lanen, Baldwin, and Riker, 1940, 1952). Duggar and Riker (1940) found that treatment of the progeny of a single, partially attenuated bacterium with ultraviolet light to the "99% kill level" would restore their virulence. Ultraviolet irradiation of virulent, or of fully attenuated, populations was without effect on the virulence or avirulence of the survivors.

The loss of virulence by glycine passage has been confirmed by Stapp (1951) and by Rack (1953). The results of Stapp and of Rack are, however, somewhat at variance with those of Van Lanen. Rack reported that glycine treatments rendered the bacteria completely avirulent for tomato plants. Neither initiation of a tumor above the site of inoculation of these bacteria, nor the addition of IAA to the host, resulted in tumor formation. The most reasonable postulate is that Rack had inadvertently selected from the glycine medium a colony which was completely avirulent rather than attenuated. Bearsley (unpub.) found that glycine-attenuated bacteria would induce tumor formation on carrot slices if the tissue was supplied with IAA. Stapp's results are of considerable importance. He showed that bacteria attenuated by glycine, alanine, or leucine were not virulent for one host although they retained their virulence for other hosts. Thus, a culture passed through many transfers on alanine medium did not induce tumors on tomato and geranium, showed reduced virulence for sunflower, and was still fully virulent for *Datura*. Unfortunately, Stapp did not study the effects of growth substances on the plants in which the bacteria were ineffective or had reduced virulence. He inadvertently may have selected specifically avirulent cultures for his tests.

With this information at hand, we can examine those reports on the inhibition of tumor-cell formation by suppression of auxin metabolism. Presumably, during the promotion phase, inhibition of auxin synthesis or utilization would prevent the conversion of normal cells into primary tumor cells, (or, according to Braun's interpretation, the stimulation of tumor cells to division) by altering the effective concentration of auxin or by interfering with its utilization. Data on this point are conflicting. DeRopp (1950) reported that certain antiauxins were effective in preventing tumor formation when applied during the first four days after inoculation. Waggoner and Dimond (1953) found that maleic hydrazide, a reputed antiauxin, suppressed tumor formation in carrot slices but did not prevent it in tomato plants. Manil and Straszewski (1952) and Klein and Klein (1952) found, however, that concentrations of maleic hydrazide which reduced the vegetative growth of tomato or *Datura* plants by about fifty per cent had no effect on tumor initiation.

Skoog (1935) and Gordon and Weber (1950, and unpub.) have shown that at low dose levels of ionizing radiation the ability of plants to synthesize auxins is irreversibly destroyed, and at still lower dose levels the inhibition of auxin is spon-

taneously reversible. Levin and Levine (1918, 1922) found that x-rays, gamma rays, and beta rays were effective in preventing tumor formation when given at or within 48 hours of inoculation. Stapp and Bortels (1933) obtained similar results. Dimond (1951) and Waggoner and Dimond (1952) examined the effects of ionizing radiation on transformation. They found that when inoculated tomato plants were given 80 r of gamma radiation per hour for a 15-day period, no tumors were evident. The bacteria were virulent within the plant at the end of this period. Doses of 500 r prevented tumor formation when given before, at the time of, or after inoculation of tomato plants. They reported that suppression of tumor formation was associated with suppression of the growth of the host.

The growth substances which act as promoting agents on cells altered by TIP (or, according to Braun, on tumor cells), may come either from (1) the incipient tumor cells themselves (or, according to Braun, from tumor cells), (2) normal tissues of the host, (3) the bacteria, or (4) several or all of these. Braun (1954) is of the opinion that tumor cells acquire, as a result of their alteration by TIP, the capacity to synthesize greater than regulatory amounts of growth-regulating substances. He has interpreted the differences in tumor formation by virulent and attenuated cultures of crown-gall bacteria in tumors as differences in the ability of the bacteria to alter the host cells relative to their capacity to produce auxin. Under these conditions, attenuated bacteria would not alter normal host cells to the same degree as do fully virulent bacteria, the weakly altered cells producing insufficient auxin for optimal cell division. When weakly altered cells are supplied with auxin, such promotion is achieved and rapidly dividing tumor cells are formed. According to the interpretation used in this review, the difference is due to the unequal capacity of the virulent and attenuated strains to effect promotion of an incipient tumor cell into a primary tumor cell.

To some extent, the findings of Stapp (1951) on host-specific attenuation support the latter interpretation. One could postulate that *Datura* cells are fully altered by the carcinogenic products of the bacteria attenuated by alanine, that sunflower cells are only partially altered, and that tomato cells are insufficiently altered and cannot produce the requisite amounts of growth substances necessary for promotion. This implies that attenuation involves a modification in the TIP-synthesis mechanisms of the bacteria, this modification being either qualitative or quantitative. It may also indicate that hitherto unsuspected etiological agents are active during the Induction Phase of the Transformation Period.

It seems unlikely that the promoting (stimulating) agent normally comes from healthy tissues adjacent to the sites of inoculation. Were this true, growth substances would not have to be supplied to tissues inoculated with attenuated bacteria, since the normal tissues would supply them in any case. An apparent exception to this supposition is found in instances where attenuated bacteria are inoculated into tissues adjacent to a bud or other meristem where the auxin gradient is high. These areas of high endogenous auxin are not, however, obligatory sites for tumor formation after inoculation of virulent bacteria and may, for our purposes, be considered as making available an exogenous supply of growth substances.

The information available at present suggests that the more likely source of the promoting agent (stimulating agent) is the bacterium. It has been shown that the events and processes involved in the conditioning of normal host cells are completely independent of the bacteria (Braun, 1952) and probably that TIP is synthesized by attenuated bacteria (Klein, 1953). Thus, incipient tumor cells may be presumed to be formed by the action of wound sap and by the TIP formed by attenuated bacteria. Since a growth substance is the only known agent which must be supplied to an incipient tumor cell to transform it into a primary tumor cell (or to stimulate a tumor cell to divide), it follows that fully virulent bacteria form these substances in vivo, whereas attenuated bacteria either do not synthesize sufficient auxin or sufficient amounts are not made biologically available for promotion.

Locke, Riker, and Duggar (1938) reported that apical dominance over the development of axillary buds of decapitated plants (a function of auxin concentration) could be maintained by exogenous supplies of IAA or by inoculation with virulent bacteria, but not by inoculation with attenuated organisms. It is not clear whether this report indicated that auxin synthesis or lack of it by the bacteria was a function of the auxin formed by tumor cells resulting from inoculation with the virulent bacteria. An inoculation of hosts with bacteria which are specifically avirulent for those hosts should answer this question. Both virulent and

attenuated bacteria are capable of multiplication in vivo (Nemec, 1930). Link and Eggers (1943, and unpub.) used the *Avena* coleoptile technique to make a time-course study of the auxinic activity of control, of punctured, non-inoculated, and of punctured, inoculated hypocotyls of tomato plants of known genetic constitution, age, and cultural and nutritional history. They found a decrease in the auxinic activity for the punctured hypocotyls after 24 hours and a rise above that of the control from the 24th hour to the 72nd hour, when the maximum was reached. They also found an increase of activity for the inoculated, punctured hypocotyl which reached its maximum titer in 24 hours and then decreased steadily until the ninth day to the level of the control. The initial decrease in auxinic activity of extracts of the non-inoculated, punctured hypocotyls may be due to destruction and injury of cells; the rise after the initial fall, to enhanced production of auxins (cf. Bloch, 1941) by cells responding to the injury. The immediate rise of the auxinic activity of extracts of the inoculated hypocotyls suggests that auxins derived from the bacteria or from host cells due to bacterial action more than offset the initial fall in auxinic activity due to wounding. More recently, Skoog (1954) has stated that bioassays of plants inoculated with attenuated bacteria indicated that the auxin in the tissues decreased relative to auxin levels in control plants. This preliminary report strongly suggests that attenuated bacteria may form an antiauxin which effectively reduces the available level of the promoting (stimulating) agent.

Direct demonstrations of the relative rates of auxin synthesis by fully virulent and sister attenuated cultures of crown-gall bacteria have been made. Locke, Riker, and Duggar (1939) reported that both attenuated and virulent bacteria produced auxin in peptone-tryptophan media, although the rate of auxin synthesis by the attenuated bacteria lagged behind that of the virulent culture for the first few days. Link et al. (1937) and Locke, Riker, and Duggar (1938) reported that virulent bacteria could make auxin in media lacking tryptophan (an auxin precursor, Larsen and Bonde, 1953), although they formed more auxin in its presence. Dame (1938) made similar observations. He also found that certain strains of his avirulent bacteria formed little or no auxin in the absence of tryptophan and only relatively small amounts in its presence. Skoog (1954) stated that attenuated bacteria not only produce large amounts of IAA in the absence of added tryptophan but that they also form a substance which interferes with the bioassay for IAA. This finding, together with his previously mentioned observation that IAA levels in tissues inoculated with attenuated bacteria decreased, suggests that attenuated bacteria are such because they prevent the incipient tumor cells from using the IAA which is made available to them. This important finding and conclusion have not yet been confirmed.

Histologically, promotion (stimulation) is marked by enlargement of the incipient tumor cells (tumor cells). In tomato stem tissues, this enlargement is clearly evident within two to three days after inoculation (Riker, 1923; Link, Wilcox, and Link 1937; Buvat, 1943, 1945; Klein, 1952; Klein and Link, unpub.). Disappearance of secondary wall thickenings is evident in tomato within 60 hours, and within 48 hours in broad bean (Rasch, unpub.). Dame (1938) observed that cell enlargement always preceded any evidence of cell division in the histogenesis of tumors in the sunflower. Riker (1926) noted that the nuclei of these enlarged cells stained deeply with basic dyes. Klein, Rasch, and Swift (1953) made similar observations on the broad bean. This is a possible indication of the synthesis by the cells of nucleic acids prior to cell division and has been noted in predivision states in many auxin-treated tissues. Klein, Rasch, and Swift (1953) have shown that desoxyribonucleic acid synthesis occurred in host cell nuclei during the Promotion and Completion Phases, about 48 hours after inoculation. Cytoplasmic modifications of the affected cells, including loss of chlorophyll, decreases in the size of plastids, etc. (Buvat, 1945), are evident at this time.

There are few data on the physiological and biochemical modifications of the affected cells which accompany promotion (stimulation). Link and Goddard (1951) found an increase in the rate of oxygen uptake two to four days after inoculation, and Klein (1952) reported increases in the concentration of total phosphorus at this time and a large increase in the level of organically bound phosphorus compounds. Protein synthesis was evident at this time as well as mobilization of nitrogenous precursors into the affected tissues (Knupp, unpub.). The increase in protein paralleled the increases in ribonucleic acid (Klein, Rasch, and Swift, 1953).

At present there is no information to indicate the presence or activity of other specific etiological agents which operate in the transformation of a normal into a primary tumor cell. If they exist, it appears most probable that they are formed either in the tissues of the host or in the prospective tumor cells themselves. It has been known for some time that there may be differences in the rates of growth and in the gross morphology of tumors incited by a single strain of crown-gall bacteria in different loci of the same host plant. Although some of these differences may be ascribed to altered nutrition states in different parts of a plant (Link et al., 1953), there are good indications that the potentialities for organization, differentiation, and growth of prospective tumorous cells are related to their position in the plant (Braun, 1953). Appler (1951) obtained larger tumors when the bacteria were placed on decapitated shoots of sunflower than when inoculated into young stem tissues. A thorough study of this phenomenon has been made by Braun (1953). These position effects probably are functions of the age of the tissues, and of the past history of the cells and of the internal environal factors, all of which probably are causally related to the specific morphogenetic potentialities of the affected cells (Link, 1933; Rose, 1953).

The positive findings of the discussion of the Promotion and Completion Phase may be summarized as follows: The etiological complex of the promotion and completion phase includes the predisposition of the incipient tumor cell to be acted on by factors and agents which promote its change into a primary tumor cell (stimulate it to enlarge). Auxin is the only agent known to do this. The natures and roles of other components of the causal complex are not known. Presumably hereditary, past history, internal and external environmental factors also play roles in the predisposition of the incipient tumor cell to be promoted into a primary tumor cell (to be stimulated to enlarge) and in the disposition and predisposition of the bacteria and affected host cells to produce auxins. The auxin necessary for promotion apparently is a product of the activity of the bacteria; and attenuated strains are less virulent because of their lesser ability to make available the proper auxins in proper amounts at the proper place and time. Possibly some auxins are formed by the incipient tumor cells (tumor cells) or by cells adjacent to them. Abnormal cell enlargement is the only visible evidence of the promotional change. Some biochemical changes are detectable at this stage.

Role of the Time Factor in Primary Transformation

In the preceding discussion of the time relations of the etiological agents that are active during the Transformation Period, emphasis was placed on the minimum time necessary for their action. It was shown that conditioning, the formation of incipient tumor cells through the action of TIP, and promotion (stimulation) of these cells by growth substances can alter a normal cell within about 36 to 48 hours after the inoculation of virulent bacteria into susceptible tissues. There are indications, however, that these lengths of time are insufficient to allow more than a minimal transformation of normal cells. By subjecting the "host-parasite complex" of *Vinca rosea* to high temperatures (45°–47°C.), Braun (1943) was able to kill the bacteria at any desired time after their introduction into the plant. He found that tumors formed following a 2-day infection period characteristically remained very small, while tumors initiated by three or four days of bacteria-host contact prior to sterilization were comparable in size and rate of growth to tumors which still contained crown-gall bacteria. The finding that tumor tissues can be freed of the inciting bacteria by heat treatments has been confirmed by White (1945a), Theis, Riker, and Allen (1950), and Klein (cf. Braun, 1951).

Braun and Mandle (1948) observed that inactivation of TIP, by holding the plants at 32°C., prior to elapse of 36 to 48 hours after infection prevented the development of tumors of even moderate size. At least 60 hours were required for the induction of large tumors. Braun (1951a) repeated his earlier studies on *Vinca*, and compared 34 and 96 hours of bacteria-host contact prior to heat sterilization of the tissues. Cells transformed in 96 hours formed large, vigorously growing tumors, while those cells which received only 34 hours formed small, slow-growing tumors. Braun noted that normal bud development at sites adjacent to these small tumors apparently accelerated their growth. This finding would suggest that death of the bacteria prevented more than a minimal promotion (stimulation) by auxin. When fragments from sterile, rapidly growing or slow-growing tumors were transferred to culture media, they maintained their characteristic growth rates. When graft-transplanted into healthy plants, these differences in growth were still apparent. Additional supplies of growth substance to the slow-growing tumors in vitro resulted only in the forma-

tion of root primordia in the tumor mass, and not in any permanent increase in their ability to grow. The tissue cultures of tumor cells altered in 96 hours were not stimulated by growth substances. These findings suggested to Braun that the action of the known etiological agents on normal cells must require a certain minimal time to produce any effect, and a longer time for superminimal effects. Thus, crown-gall tumor cells possessing a minimal transformation are capable of normal morphogenetic and organizational responses under the influence of known compounds which can exert regulatory actions.

Fig. 6 shows the time interrelations among the

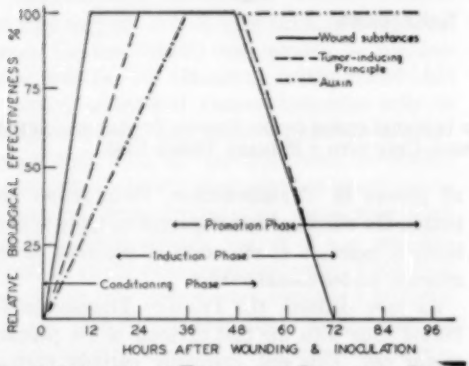

FIG. 6. RELATION OF TIME TO THE BIOLOGICAL EFFECTIVENESS OF WOUND SUBSTANCES, TUMOR-INDUCING PRINCIPLE, AND GROWTH SUBSTANCES IN THE PRIMARY TRANSFORMATION OF NORMAL TO PRIMARY CROWN-GALL TUMOR CELLS

etiological agents known to be active during the period of primary transformation. Following wounding of host tissues, wound substances, possibly wound-auxins, activate resting cells, these cells becoming fully conditioned within 12 to 24 hours. The conditioned cells remain fully disposed to subsequent tumor-inducing actions until about 72 hours. When the cells are conditioned, they may be acted upon by TIP and, when so altered, can be promoted (stimulated) by growth substances. In each instance, the cells must have been rendered positively predisposed to the action of the succeeding etiological agent. Further, the agents must be made available in sufficient amounts, or must possess sufficient biological effectiveness, to permit optimal transformation. Any reduction in the time of action of any of these agents or factors will suppress or prevent optimal transformation of the cells.

The implications of these hypotheses are clear. Cellular autonomy may be acquired within the 36- to 48-hour period following wounding and introduction of the bacteria. Acquisition of the capacity for tumorous growth behavior requires additional time, and transformation is only minimal unless the gradual acquisition of these characteristics is permitted.

Summary of the Primary Transformation Period

A diagrammatic summary of the sources and interrelations of the known etiological agents which, in series, are responsible for the transformation of normal cells into primary tumor cells is given in Fig. 7. The first of these agents, grouped for convenience, are termed wound substances. Some of these may be "wound-auxins." They are evoked by or are derived from cells injured or ruptured by wounding. They act on healthy cells during the Conditioning Phase, altering them in some unknown fashion into *conditioned cells*. Crown-gall bacteria are not required for these alterations, and the processes are not absolutely temperature-dependent. Without subsequent exposure to other etiological factors and agents, the conditioned cells probably would be integrated into callus or into other wound periderm tissues (cf. Magnus, 1918; Klein, 1954). This suggests that the conditioning process is not specific for crown-gall genesis. Conditioned cells may, however, be considered as having acquired a positive disposition to the action of the factors and agents operating during the following phases of the Transformation Period.

In the Induction Phase, conditioned cells are acted upon by a tumor-inducing principle which appears to be a metabolic product of virulent and of attenuated crown-gall bacteria. This principle may be a specific desoxyribonucleic acid synthesized in effective quantities only in the presence of wound substances and formed only by those bacteria which possess or have acquired the proper hereditary constitution. The available amount of tumor-inducing principle is rigidly temperature-dependent, the principle being inactivated or not synthesized above 32°C. In the Induction Phase, as in the Conditioning Phase, no specific structural modifications of the affected cells are apparent, although certain biochemical changes indicate that the cells are metabolically more active than resting cells. The resulting *incipient tumor cells* (tumor cells), although not fully capable of the autonomous growth behavior characteristic of crown-gall tumor cells, may be considered as having acquired

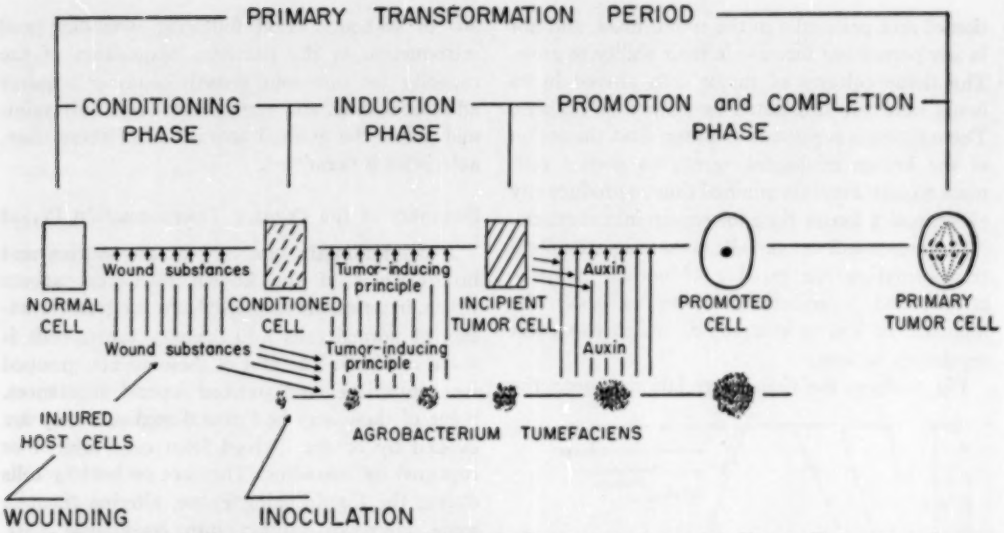

FIG. 7. DIAGRAMMATIC REPRESENTATION OF THE PRESUMED INTERRELATIONS OF THE KNOWN ETIOLOGICAL AGENTS IN THE PRIMARY TRANSFORMATION OF A NORMAL CELL INTO A PRIMARY TUMOR CELL

a more or less permanent "bias" or "propensity" towards the tumorous state.

The etiological agents which translate this bias into an actuality act on incipient tumor cells (tumor cells) during the *Promotion and Completion Phase* (Cell Stimulation-Cell Enlargement Phase). Growth substances are the only agents now characterized which act during this phase. They appear to be synthesized by virulent crown-gall bacteria but possibly may also be derived from the incipient tumor cells themselves or from adjacent cells. Cells in this phase are marked by an increase in cell volume and by other cytological and biochemical changes. The existence of other specific etiological agents which act on the *promoted cells* has not been demonstrated. If such exist, they are probably derived from the promoted cells or the tissues of the host, since the crown-gall bacteria are not required at, or subsequent to, the end of the Transformation Period.

Our knowledge of the existence, sources, and modes of action of these etiological agents is better than our knowledge of the role of intrinsic etiological factors such as the genetic constitutions of host and pathogen, the internal environal factors and past history effects, and of other external environmental influences, such as light, etc. That they are important limiting factors in tumor-cell formation is obvious, but the lack of data precludes any detailed summary of their effects on the process. They seem to act during all phases of Transformation, their action and that of the effects of and responses to these actions being a function of the state of the cells at the moment under consideration.

As here defined, the Primary Transformation Period ends with the first division of the primary tumor cell. This cell, originally entirely normal, has been followed from the time of the wounding of the host until the preparation of the cell for division. (If Braun's proposition proves to be the correct one, then the cellular changes considered in this review to belong to the promotion and completion phase of the Transformation period will have to be considered as the initial phase of the Duplication period and may constitute a Cell Stimulation-Cell Enlargement Phase followed by a Cell Division Phase.)

INITIATION STAGE OF A SECONDARY TUMOR

Primary Transformation of Secondary Tumors

Smith (1911, 1922, 1923) reported finding in the Paris Daisy and in other plants masses of tumorous cells which "extend rootlike" from the primary tumor into tissues of the host, and, at various places, proliferate into one or more "secondary tumors." He considered these supposedly infiltrating structures to be the equivalents of permeation metastases of animal cancers. These findings and his explanation of them were the basis for his conclusion that crown-gall is a plant cancer and for his hypothesis that animal cancers

might be of bacterial causation. Smith's findings and his conclusions led to a series of conflicting findings and conclusions by others. Pelco (1915) observed connecting strands between some primary and secondary tumors. Küster (1915), on anatomical grounds, concluded that Smith had not proven that the strands arose by infiltrating growth from the primary tumor. Riker (1923b) and Robinson and Walkden (1923), as well as many other workers, questioned the existence of tumor strands, and stated that elongated chains of tumor cells arose only by divisions of tumorous cells along the channels of bacterial movement. It was shown that the bacteria can move passively for some distance through the vascular elements and may migrate as a zooglea through compacted tissues. Levine (1925a) was unable to see any tumor strands, but Gäumann (1946) stated that in young, unlignified tissues tumorous cells in the xylem region may force themselves between normal host cells by interpositional (intrusive) growth. Braun (1941) photographed small tumor strands but demonstrated that these were quite limited in their growth and were not root-like extensions of the primary tumor mass. They were initiated in the xylem and expanded laterally into the pith. No strand tips, comparable to rootlets, could be found. It is of interest that many, but not all, of these strands were free of crown-gall bacteria. DeRopp (1951c) pointed out that metastasis, in the sense used by oncologists, is impossible in plants possessing neither a circulatory system nor wandering cells. Furthermore, the rigid scaffolding of cellulose walls also tends to rule out metastasis.

Following the demonstration that secondary tumor formation more than a few centimeters removed from the primary tumor is unlikely to be originated by the development of tumor strands, some explanation had to be found for those secondary tumors which are formed ten to twenty centimeters above or below (Stapp, 1947) the primary tumor. Riker (1923b), Robinson and Walkden (1923), Magrou (1928), Hamdi (1932), and others have reported that these arise when the primary inoculation is made into the apex of a stem containing condensed nodes and internodes. It was assumed that the bacteria, carried in wound sap, are thus distributed throughout these tissues and transform the host cells prior to eventual separation by the normal elongation of the axis. Riker (1923a) reported that crown-gall bacteria can move passively and freely within liquid channels created by the wound sap. This finding was confirmed by Ivanoff and Riker (1930), Suit and Eardley (1935), and Stapp, Müller, and Dame (1938). DeRopp (1948d) found that bacterial migration through isolated stem fragments was not affected by the polarity of the tissue. Robinson and Walkden (1923) and Hill et al. (1928, 1930) reported that the bacteria move only as zoogleal masses in intercellular spaces, observations which Suit and Eardley (1935) and DeRopp (1948d) could not repeat. During the early portion of tumor genesis, zoogleal bacterial masses probably do not exist. Therefore, according to this hypothesis, secondary tumors really are primary tumors (Levine, 1936b) and "tumor strands" result from primary tumor cells and their progeny when they are "pulled out" into strands during elongation of the stem. This hypothesis accounted for the reported connections between "primary" and "secondary" tumors (Pelco, 1915).

In 1935, however, Suit and Eardley reported secondary tumors on young apple twigs, a phenomenon not in conformity with the elongation hypothesis. These writers explained their secondary tumors by assuming that the bacteria migrated up the twig in the xylem (removal of phloem by girdling did not prevent secondary tumor formation) and induced tumor formation near procambial strands where vessels had been ruptured during normal growth processes. Riker, Spoerl, and Gutsche (1946) have explained several other instances of secondary tumor formation by this hypothesis.

Secondary Transformation

Although these explanations appear to cover adequately many cases of "secondary tumor" formation, Braun (1941) reported a series of experiments on the sunflower the results of which do not fit into these hypotheses. The hypothesis based on the elongation of non-elongated internodes was eliminated by inoculation of fully elongated internodes which were up to six inches from the apex. Secondary tumors were found even under these conditions. Secondary tumors could also be found below primary tumors. The migration and growth injury hypothesis was eliminated by two sets of experiments. First, secondary tumors could appear as late as a month after the appearance of the primary tumor at sites on the plants which at the time of tumor appearance were some distance from the apex or

even from procambial strands. Second, secondary tumors were formed following inoculations of attenuated crown-gall bacteria which did not induce primary tumor formation. As additional support for his suggestion of a new mechanism of secondary tumor formation, Braun reported that the secondary tumors were morphologically different from the primary tumors. Of major significance was the observation that many of the secondary tumors were free of bacteria. In no case did tumor strands connect the tumors, morphologically normal tissues lying between the two. The last finding has been confirmed by Hamdi (1930) for sunflower and by Link et al. (1953) for tomato (see Fig. 5). Braun examined the possibility that the bacteria may have traveled up the stem to the site of the secondary tumors, but the finding that these were sterile, and the fact that the inoculation of attenuated bacteria induced secondary but not primary tumor formation, tended to eliminate the hypothesis of Suit and Eardley. It is probable that if bacteria were present in the vessels, they remained confined therein and formed substances which moved laterally, inducing secondary transformations in vascular-associated tissues. Essentially similar mechanisms can be postulated for tumor strand formation. These hypotheses were severely criticized by Riker, Spoerl, and Gutsche (1946), but no experimental evidence was presented by them to refute Braun's conclusions.

The report that many of these secondary tumors were bacteria-free suggested that their tissues were well suited for studies of the supposed autonomous growth of tumor tissues. White and Braun (1941, 1942) isolated tissues from the secondary tumors, grew them in vitro, and demonstrated conclusively that they were sterile (cf. Braun and White, 1943). These tissues grew in vitro at relatively rapid rates and did not require any exogenous supply of growth factors. They could be grafted back into healthy plants where they continued to proliferate as tumors, although grafts of normal tissue fused with the host. These findings have been confirmed by Braun and Morel (1950) and by Lance and Gautheret (1952). Growth in vivo of the grafted tumors appeared to be mainly if not wholly from the transplant. Cell-free macerates of these tumor tissues were incapable of inducing tumor formation upon injection into plants. Thus, if the abnormal proliferative capacity was due to a virus, it could not be of the easily transmitted type, such as tobacco mosaic. It is clear that secondary tumor formation, at least in some cases, occurs through the activity of etiological agents derived from primary tumor tissues or from bacteria not in intimate contact with the tissue to be affected. These agents must be capable of acting at a distance from the infection court of the bacteria or from the primary tumor. Since it is doubtful that wounding of the tissues is a factor in this type of secondary tumor formation, it must be concluded that secondary tumor cells are formed by different mechanisms than those involved in primary tumor-cell transformation. The resulting tumor tissues appear to be physiologically and biochemically identical with sterile tissues from primary tumors. They possess the same growth characteristics and autonomous behavior in vitro. Although the mechanisms of transformation are different, the two types of tumor cells are apparently the same. DeRopp (1947c) demonstrated that sterile tissues of primary tumors of sunflower showed the same characteristics, and other workers subsequently isolated sterile tissues from primary tumors of other hosts.

Although there is no longer any doubt that cells of the primary tumor and their progeny are capable of autonomous growth behavior both in vivo and in vitro, the problem still remains whether these cells can transmit the property of tumorous behavior to adjacent normal tissues. Not all the evidence available from the studies dealing with secondary tumors in vivo bears on this problem, because crown-gall bacteria were occasionally present in the plants under examination. Magrou (1927) and Brown and Gardner (1937) concluded that gall-stimulating substances produced by the bacteria were responsible for secondary tumor formation, but it is most likely that they were considering the formation of non-autonomous neoplastic tissues induced by growth substances derived from the primary tumor. Jensen (1910, 1918) isolated bacteria-free tumor tissues from beets. He reported that the bacteria provided only the initial stimulus for tumor-cell formation, the stimulated, non-infected cells having become autonomous. When he grafted sterile tumor tissues of red beet into yellow beets, the resulting tumor mass developed only from cells of the implant, and never from contiguous host cells. There was, moreover, no deep penetration or infiltration of tumor tissues into the host. White and Braun (1942) showed that tissues of secondary tumors of sunflower were autonomous

in vitro and following in vivo grafts, but they were unable to obtain any extensive tumorous modification of the host cells adjacent to the grafted tumor tissues. There were hypertrophies of the xylem of the host adjacent to the graft which these investigators stated were due to mechanical strains set up in the presence of the proliferating tumor mass. It is possible that growth substances diffusing from the tumor induced this hypertrophy or that the hypertrophied cells may have been truly tumorous. White (1945a) isolated tumor tissues from heat-treated *Vinca* plants. When these sterile primary tumor tissues were grafted back into healthy plants, they grew into typical crown-gall tumors. These tumors apparently arose from the implant and not from host cells.

Additional findings bearing on the problem of secondary transformation are derived from observations pertaining to appositional growth of primary tumors. Smith (1922) reported that examination of histological preparations of tumor-bearing stems of Paris Daisy and other plants revealed a zone of cells between the tumor cells and the normal cortical cells which were, in size, shape, affinity for tumor stains, and proliferative capacity, intermediate between tumorous and normal cells. This phenomenon, which he termed *appositional growth*, Smith thought involved the conversion of normal cells into tumor cells by contact, "... that is, peripheral extension of the tumor further and further into the cortex by conversion of the adjacent normal cortex cells into tumor cells." Cells of the appositional growth zone possessed thin walls, enlarged nuclei, and in some cases, as many as sixteen small tumor cells were present within the stretched and thickened walls of the parent cortical cell. Similar findings were reported by Riker (1923b), Purr (1938), Buvat (1945), and Klein and Link (unpub.) for tumor tissues of tomato during the early part of the Duplication Period. These tumor cells formed by appositional transformation appeared to be exactly like young primary tumor cells. Beyond the appositional growth zone was found a zone of cortical cells which were slightly larger than the normal cells but were otherwise morphologically unaltered. Examination of Smith's photographs shows that the histological changes in the zone of appositional transformation are unlikely to be wholly due to the action of growth substances diffusing from adjacent primary tumor cells. Since primary transformation processes do not occur once wound-healing has been completed, these findings may be interpreted as indicative of secondary transformation processes involving the interaction of tumorous and normal cells (see Fig. 4).

A second line of evidence for secondary transformation in crown-gall genesis has been presented by DeRopp (1947b, 1948a). When fragments of sterile sunflower tumor tissues were grafted onto isolated segments of healthy stems (homoplastic, in vitro grafts), two types of responses were noted in the stems. The first involved the formation of roots and masses of hyperhydric tissues resembling neoplastic tissues induced by growth substances. The second response was the formation of crown-gall tumors which equalled or exceeded in size the original fragment of tumor tissue. In one instance, the secondary tumor appeared at the end of the stem fragment opposite the implant of tumor tissue. These secondary tumors were initially characterized by a somewhat more regular internal structure than the implanted tumor tissue. If the primary tumor graft was separated from the healthy stem tissues by a thin layer of agar, no secondary transformation occurred. Neoplasms induced by growth substances, on the other hand, are readily induced by diffusion through agar. The failure of previous workers to obtain secondary tumor formation by graft apposition may be due to their use of intact plants as stocks. Under these conditions, morphogenetic influences of the host could modify the reaction of stock and tumorous scion. DeRopp (1948a) noted that only certain strains of tumor tissue were active in inducing secondary tumors. These graft-induced secondary tumors could grow in vitro at rates comparable to the inducing primary tumor tissues. After several transfers in vitro, tissues derived from these secondary tumors lost their regular structure and appeared similar to those of cultures of primary tumor tissue. Injection of extracts of tumor tissue into healthy stems, wounding, or treatments with growth substances did not induce secondary tumor formation. These results show that the new tumors are unlikely to be due to auxins or that they arose as a result of wound stimuli. Migration of grafted tumor cells to the site of secondary transformation is also improbable because of the rigidity of the tissues; and the structure of the secondary tumors suggests that it was unlikely that the new tumor was derived by proliferation of one or more primary tumor cells. The autonomous growth behavior of the excised secondary tumors

in vitro further indicates the true tumorous character of the tissues.

The experiments of DeRopp have been confirmed by Camus and Gautheret (1948a), using tissues of the Jerusalem artichoke and by McEwen (1952), using sunflower stem tissues. These workers demonstrated that the secondary tumor grew in vitro on a medium which permitted excellent growth of tissues of crown-gall but did not support the growth of normal tissues or of auxin-induced neoplastic tissues. DeRopp (1951e) concluded that a factor capable of transforming healthy cells adjacent to tumorous cells by contact is present in tumor tissues free of the inciting bacteria.

It has been shown that primary transformation requires the presence of wound substances, a factor (TIP) synthesized by the bacteria, and growth substances. The transformations which result in secondary tumors do not appear to require wound substances, nor do they require the presence of the bacteria in intimate contact with the cells. In appositional transformations, wound sap was present at the time of the grafting, the bacteria were absent, and relatively large amounts of growth substances were available from the tumor scion. In either type of secondary transformation, the absence of the bacteria precludes the possibility that TIP is acting on the cells. Further, the appositional growth factors must be present in the tissues, and the TIP does not appear to be stable beyond the first few days after inoculation. The nature of the agents which alter normal cells adjacent to them or at a distance is still unknown. Speculation as to their possible nature has been reserved for the section dealing with the modes of action of causal agents and factors.

GROWTH STAGE OF A TUMOR

Duplication Period

With the end of the initiation stage of tumor development the growth stage is initiated, and with it, the second period of cellular change and behavior, the duplication period. From the cellular point of view, the growth stage may be considered a composite one. It includes the duplication period, characterized by multiplication of the primary tumor cells and their progeny and, if secondary transformation occurs, also the secondary transformation period of secondary tumor cells, and the period of their duplication. In dealing with all of these events and processes, it is no longer adequate or possible to follow the history of merely an individual primary or secondary tumor cell, but one must be concerned with events in a population of cells. During the duplication period, factors activated within the mass of tumor cells and within the cells and tissues of the host play increasingly important roles in the complex of events characteristic of the growth stage of a tumor.

Structure

The cytological and histological details of the multiplication of tumor cells have received surprisingly little attention. Most of the studies on cell and tissue structure have been made with mature tumor tissues (Figs. 8, 9, 10). The most nearly complete studies of the early stages of tumor growth have been made by Riker (1923b, 1926b), Buvat (1945), and Klein and Link (unpub.) for tomato crown-gall, and by Rasch (unpub.) for the broad bean. Cook (1923) studied the early stages of crown-gall on castor bean and on *Bryophyllum*, but he gave no details of the time when he took his samples. Robinson and Walkden (1923) made limited studies on the Paris Daisy. Fragmentary reports have appeared on the growth of other tumors (cf. Riker and Berge, 1953) but are too incomplete for our purposes.

In tumors on tomato stems, the first divisions of primary tumor cells are evident in parenchyma cells in longitudinal sections about 60 hours after inoculation, and in transverse sections, in about 72 hours after inoculation. Riker (1923b) reported that a few cell divisions occurred within 96 hours, the dividing cells being of cortical origin. Buvat (1945) has confirmed this report. Other workers found that when the inoculations penetrated to the pith, the first divisions occurred in enlarged phloem and xylem parenchyma cells. DeRopp (1948c) reported that the xylem parenchyma and the cambium tissues of sunflower were initially the most active tissues. Cook (1923) stated that xylem parenchyma was the first tissue system to react in castor bean. The same tissues are the most active in Paris Daisy (Robinson and Walkden, 1923), the first divisions occurring in enlarged xylem parenchyma cells within 72 hours after inoculation. In the broad bean, these changes occur about 24 hours earlier than in tomato, i.e., enlargement in 36 hours, and occasional divisions within about 48 hours after inoculation (Rasch, unpub.). Riker (1926b), Buvat

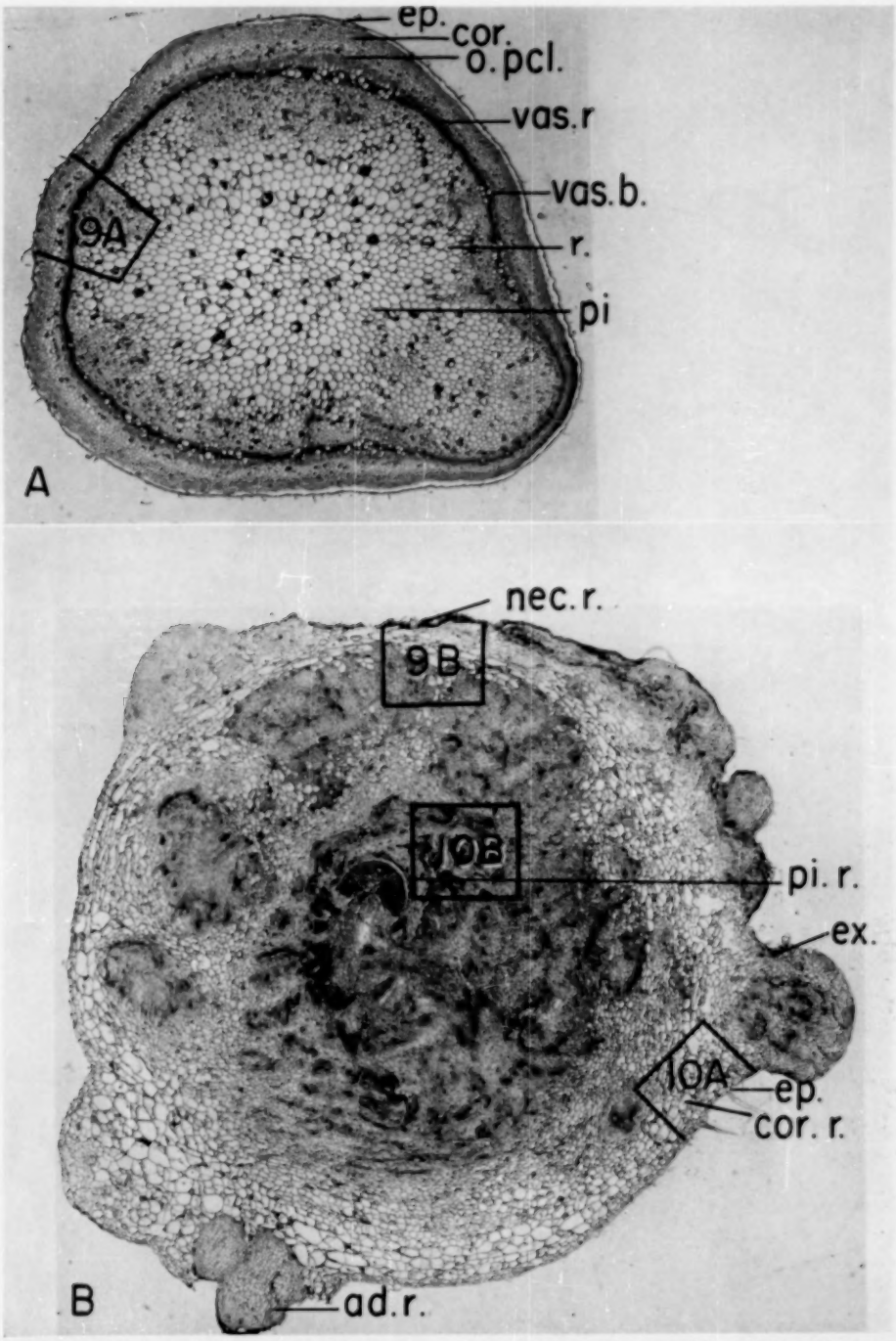

FIG. 8. TRANS-SECTIONS OF (A) INTERNODE OF NON-INOCULATED TOMATO PLANT, AND (B) OF 30-DAY TUMOR FROM EQUIVALENT INTERNODE OF A PLANT INOCULATED 21 DAYS AFTER SOWING

Rectangle A is shown enlarged in Fig. 9A, and the rectangles in B are similarly reproduced in Figs. 9B and 10A, B.

A. ep., epidermis; cor., cortex; o. pcl., outer pericycle; vas. r., vascular ring with fascicular and interfascicular cambiums and their derivatives; vas. b., vascular bundle; r., pith ray; pi., pith.

B. ex., excrescences of tumorous tissues from main tumor; ad. r., adventitious root; nec. r., necrosis of outer layers of collenchyma and epidermis. Mag. × 9.

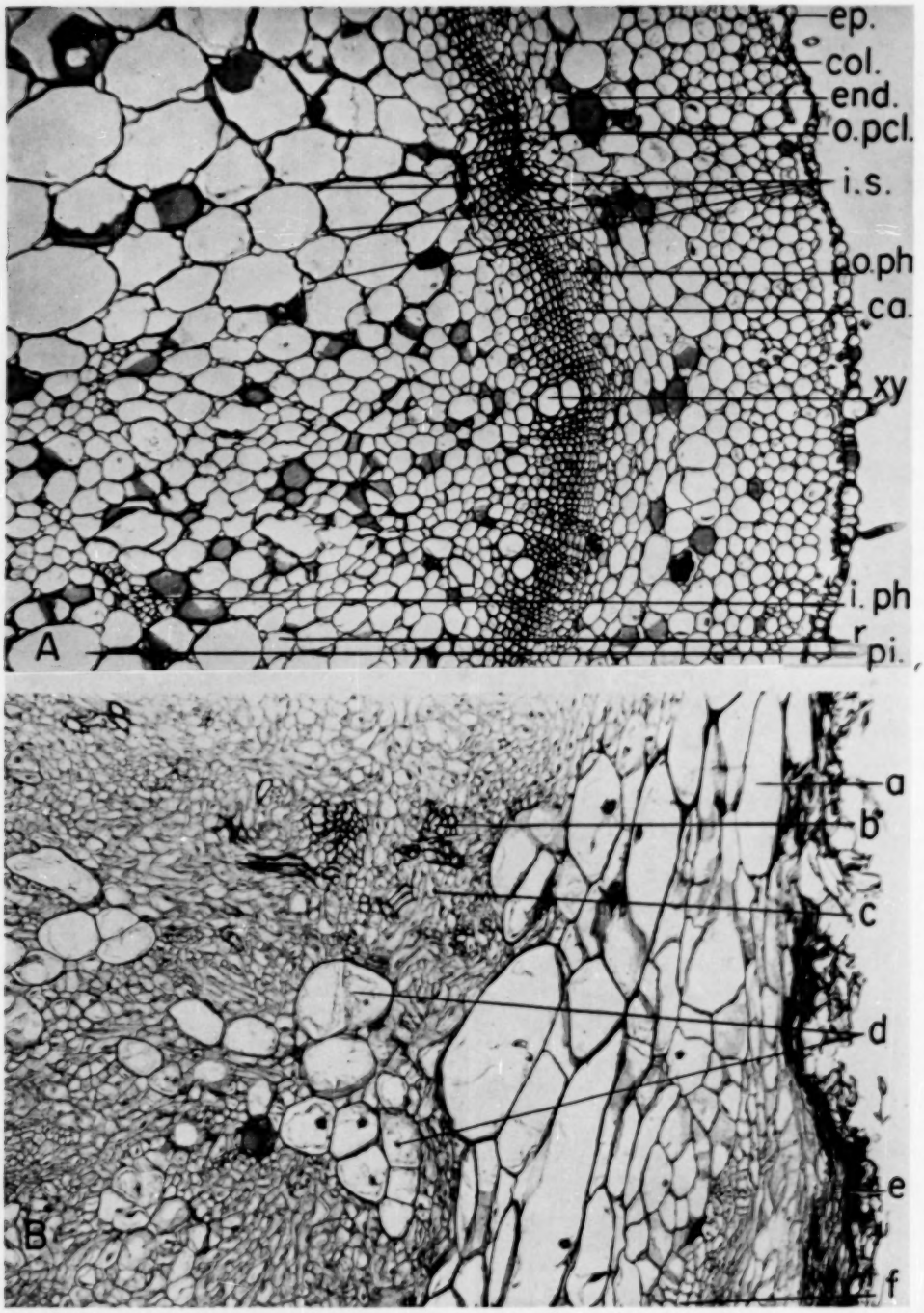

FIG. 9. DISTRIBUTION AND RELATIVE AMOUNTS OF TISSUES AND TISSUE SYSTEMS IN NORMAL AND TUMOROUS INTERNODES OF TOMATO

A, rectangle 9A from Fig. 8, A Normal. ep., epidermis; col., collenchyma; end., endodermis; o. pcl., outer pericycle; o. ph., outer phloem; ca., cambium; xy., xylem; i. ph., inner phloem; r., ray; pi., pith; i. s., intercellular space.

B, Rectangle 9B of Fig. 8, B. Inoculated. a, excessively enlarged cell; b, nest of sclerenchymatous cells, out of place; c, excessively small cells resulting from frequent division and failure of enlargement; d, excessively large cells undergoing repeated division eventually leading to cells as in c; e, necrobiotic and necrotic cells; f, nest of cells like those of c, which constitute the bulk of the tumor. Mag. × 80.

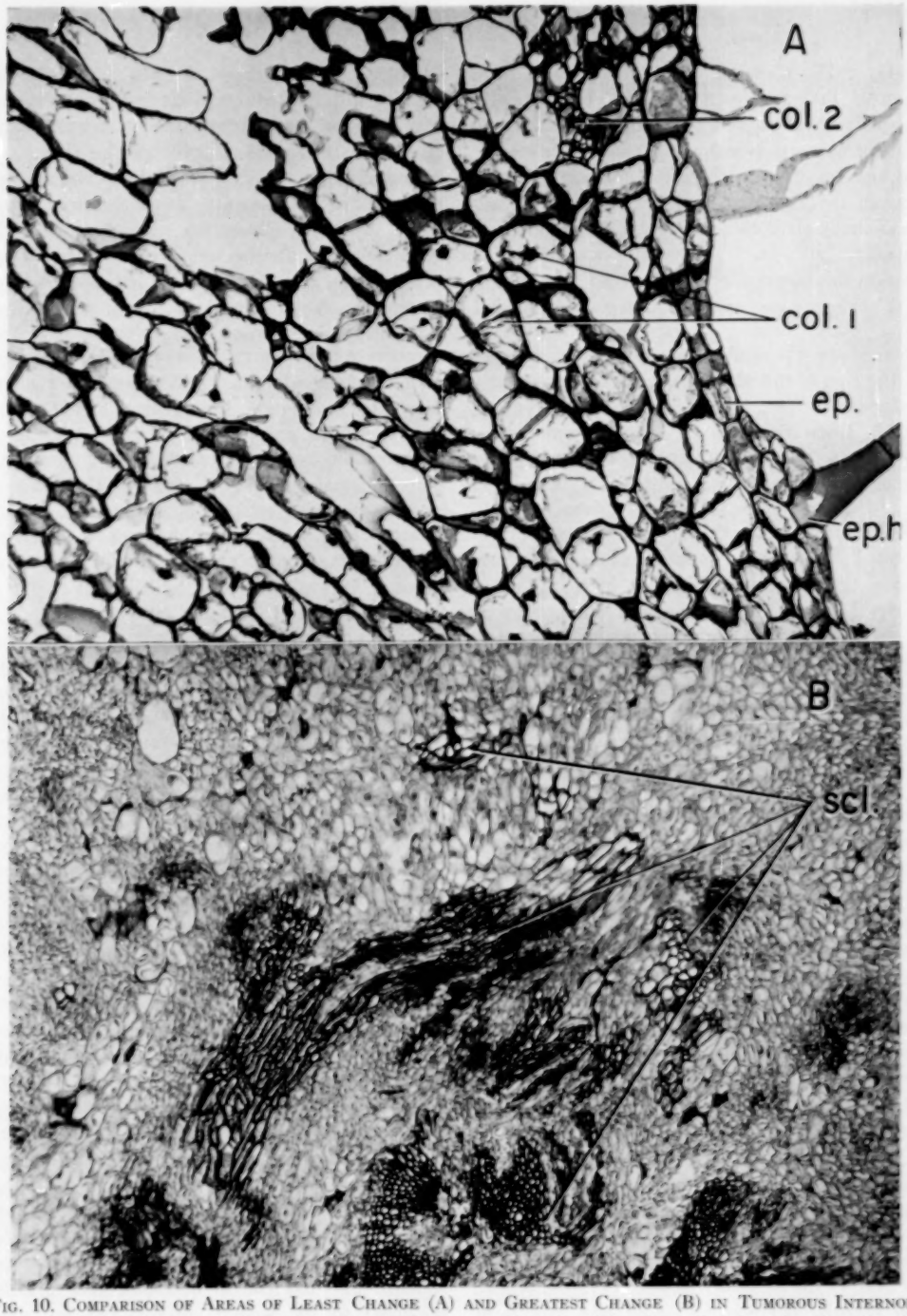

FIG. 10. COMPARISON OF AREAS OF LEAST CHANGE (A) AND GREATEST CHANGE (B) IN TUMOROUS INTERNODE

A, rectangle 10A of Fig. 8, B. ep. h., epidermal hair; ep., epidermis with cells much enlarged and undergoing periclinal and anticlinal divisions; col. 1., abnormally enlarged cell of collenchyma undergoing division; col. 2, nest of small cells from repeated divisions but with no enlargement.

B, rectangle 10B of Fig. 8, B. scl., sclerenchyma. Section devoid of intercellular spaces, and composed mainly of small dividing cells with large nuclei, enlarged cells undergoing repeated division, and abnormally distributed and organized areas of aberrant sclerenchymatous cells. Lack of normal vascularization and organization is evident. Mag. × 80.

(1943, 1945), Geneves (1946), and others have reported that the early divisions are frequently unequal, daughter cells orienting themselves so that the new wall is within a portion of the mother cell and usually near the intercellular spaces containing the bacteria. Callus tissues of tomato occasionally show this character (Klein and Link, unpub.), but Rasch (unpub.) was unable to confirm this observation in the broad bean.

It has been reported that starch grains disappear from young, dividing tumor cells. Chloroplasts, where initially present, divide repeatedly, decrease to the size of mitochondria, and may eventually disappear (Buvat, 1945; Link, Wilcox, and Link, 1937). Chondriosomes of tomato tumor cells swell, resulting in a "vascularization" of these organelles. Buvat (1945) noted that there is a true dedifferentiation of mature parenchyma to meristematic cells with intermediates of the cambial type. Inclusions of calcium oxalate, pectin, tannin, etc., may be seen in young tumor cells (Manigault, 1953). Nucleoli are prominent in the nuclei, which are proportionately larger in the small, rapidly dividing tumor cells than in mature tumor cells. Riker (1926b), however, reported that the nuclei are proportionately smaller than those in resting cells. Riker, as well as Robinson and Walkden, observed that the walls of young tumor cells stained more deeply with methylene blue and Sudan III than normal cell walls. Riker suggested that necrobiotic changes were occurring in these cells. In view of the tremendous metabolic activity of such cells, this conclusion seems unwarranted. Most workers agree that injured cells, and those cells invaded by crown-gall bacteria, usually die without division. Cytochemically, tumor cells of the broad bean are marked by increased basophilia in both nuclei and cytoplasm. Desoxyribonucleic-acid Feulgen values indicative of nucleic acid synthesis were noted at the time of the first division of bean tumor cells (Klein, Rasch, and Swift, 1953).

The young tumor mass usually becomes macroscopically evident within four to nine days after inoculation. Although some of this swelling is due to enlargement of cortical and vascular parenchyma (see Figs. 8–10), tumorous cell division accounts for most of the increased volume. In pith, cortical, and vascular parenchyma, small cells may form within parent cells (Riker, 1923b; Klein, Rasch, and Swift, 1953; Klein and Link, unpub.). Riker (1923b) observed that ensheathment of the foci of bacterial infection resulted from stimulation of the division of adjacent cells, but neither Rasch, working with the bean, or Klein and Link, working with tomato, have been able to confirm this observation. Cambial activity of the tissues of tumorous stems was evident, and cambial derivatives tended to integrate into the tumor mass rather than to differentiate normally. All cell types capable of division were actively proliferating at this time, and the tumor growth pattern was perceptible eight to ten days after inoculation of many hosts. In tomato, a general increase in the numbers of tumorous cells was seen (Riker, 1923b), with no differentiation of these cells within 16 days after inoculation. Enlargement of the tumor mass continued, and the affected tissues became so distorted and closely packed that few intercellular spaces remained (Flint, 1951). Thin-walled, rapidly dividing cells were intermingled with enlarged tumor cells which had ceased division. At this stage of tumor growth, the tumor has been called a "hyperplastic mass" by Riker (1923b) or a "tumor mass" by Klein and Link (1952).

Unfortunately, the microscopic picture of the early Duplication Period is seldom as clear-cut as has been indicated above. In some plants histological development of wound tissues parallels growth and division of the young tumor cells, and visual separation of the two types is quite difficult. In tomato, wound responses usually involve only cicatrization of the wounded area and a limited development of wound periderm. Formation of a phellem is effected by only limited cell enlargement, and divisions in this tissue are usually periclinal to the wound surface (Klein, 1952). In the castor bean and *Bryophyllum* (Cook, 1923), the situation is much the same as in tomato. In apple and other fruit trees, however, where wound-healing is effected by the formation of voluminous callus when grafts are poorly matched, the situation is much more complex. In root-grafted apple trees, irregularities in the healing of the stock and scion frequently result in overgrowths containing extensive callus and wound-callus derivatives. Superficially, these overgrowths resemble crown-gall tissue (Riker and Keitt, 1926), and some of them undoubtedly were infected in the field with crown-gall bacteria. Here, as in tomato, the first calloid divisions were usually periclinal to the wound surface, and are thus distinguishable from crown-gall tumor cells. Subsequently, callus development occurred by division in all planes (Sylvester and Countryman, 1933). Riker and Hildebrand (1934) reported that

wound callus, in contrast to crown-gall, developed rather slowly, and that the callus tended to cease growth within a relatively short time. Rasch (unpub.) made a cytological study of the early stages of tumor development and of wound responses in the broad bean. In both wounded and inoculated bean tissues, the formation of a pseudocicatrice and the origin of primary callus were essentially similar to tumor-cell divisions during the initial period of tumor growth. Many of the divisions of callus were transversely oriented and occurred in the last differentiated stelar parenchyma. Mitotic indices for wounded and inoculated tissues were the same during the first three days. After this period, however, tumor tissues rapidly outpaced wound periderm, reaching a peak of mitotic activity during the fifth to the ninth day after inoculation. Polyploid cells may participate in periderm formation, but continued division and production of polyploid cells were characteristic only of the cells in the tumor mass. Differences between tumorous responses and those involved in periderm formation appeared five or more days after wounding. Cell divisions in tumor tissues occurred in all planes, rather than in the usual periclinal and transverse planes along the line of the wound. Disorientation of already differentiated tissue elements by proliferation of the tumor mass during the Duplication Period further distinguished this growth from the organized responses of periderm formation. Abnormal divisions, with the production of binucleate cells or the appearance of micronuclei were found in cells of both types of tissue and were not considered characteristic of tumor cells (cf. Nemec, 1928).

Little study has been made of the inclusions and cytoplasmic organelles of crown-gall tumor cells. Riker (1926b) observed various crystals, mainly oxalates, and some amorphous bodies. Milovidov (1930) reported that these were tannins, a finding in which Riker and Berge (1935) concurred. Milovidov (1930) and Manigault (1953) concluded that the inclusions in tumor cells were qualitatively identical with those found in healthy cells. Banfield (1935) could not find any differences between the organelles of normal and tumorous cells except the well-known disappearance of plastids from the latter. He did note that the fixation image of the hyaloplasm of tumorous cells tended to be more "open" than that seen following fixation of normal tissues.

In contrast to the paucity of research on the cytoplasmic inclusions and organelles of tumorous tissues, the nucleus has been extensively investigated. Summaries of these studies have appeared (Riker and Berge, 1935; Levine, 1931, 1936b). Two sharply divided schools of thought arose with regard to the occurrence of abnormal and polyploid nuclei in tumor tissue. One group, led by Smith, Brown, and McCullough (1912), Blumenthal and Hirschfeld (1922), Smith (1922), Winge (1927), and Kostoff (1933a, b), asserted that high frequencies of abnormal divisions, many aberrant nuclei, and an extensive polyploid condition existed in the tumor cells relative to corresponding normal tissues. The excessive polyploidy, it was claimed, was due to non-disjunction of the chromosomes at metaphase or to nuclear fusions in the absence of cell division. According to Winge (1927) and Kostoff (1933), this polyploidy multiplied the numbers of "growth-controlling" genes per crown-gall tumor cell. It was also thought that this condition might have genetic significance in that tumors may, potentially, be tissues of new plant species.

Opposing these views, Levine (1925b, 1930, 1931, 1936b), Riker (1926b), Banfield (1935), and Garregues (1943) have reported that polyploid cells and abnormal divisions occurred with equal frequency in healthy tissues and tumor tissues. Appler (1951) did not observe any abnormal number of nuclei in cells of sunflower tumor tissues as compared with tissues treated with growth-substances. The majority of the cells of tumors, according to this group of workers, are diploid, and in contrast to Winge's (1927) suggestion, the polyploid cells arise from diploid cells and not the reverse. In 1945 Kostoff and Kendall reversed their earlier position and concluded that polyploidy is not a "cause" of tumors but may result from a certain percentage of aberrant divisions which might be expected to occur under the conditions of rapid cell division. These workers and Nemec (1928) indicated that, once formed, polyploid cells multiply rapidly. Recently, studies on the nuclear condition of cells of normal stem tissues of broad bean and of tumor cells of this host have reopened this question. Using conventional cytological techniques, Coleman (1950a, b) reported that a considerable degree of polyploidy exists in normal parenchyma cells of the cortex and the pith. In these tissues, the percentage of polyploid mitoses may be as high as fifty per cent of the total number of active cells. Tetraploid and even octoploid nuclei were common. Treatment of the normal stem

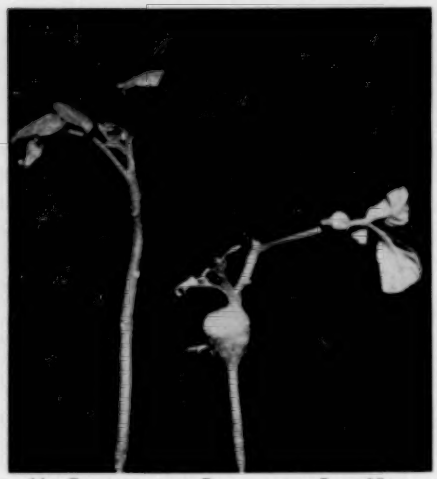

FIG. 11. CONTROL AND INOCULATED LOW-NITROGEN TOMATO SEEDLINGS

Seedlings severed at soil line for photography. Control plant, left, has maintained apical growth by progressive removal of nitrogen nutrients from lower leaves prior to their premature abscission. Plants are stunted, woody, yellow, and rigid. Tips of top leaves of control plant are dying. Plant on right inoculated near the growing point which also has begun to become tumorous. The tumor has developed an adventitious leaf on the left. Tumor grew at expense of the rest of the severely stunted, nitrogen-starved plant.

with IAA resulted in the production of polyploid tissue masses, these tissues arising from polyploid cells already in the untreated tissue. Coleman concluded that the same conditions operate in the formation of polyploid cells in tumor tissues. Klein, Rasch, and Swift (1953) determined the amounts of DNA stained with Feulgen per tumor. cell nucleus and found divisions of polyploid nuclei. There was a marked shift in the percentages of polyploid cells to the higher polyploid classes (16- and 32-ploid) with increasing age of the tumor. Rasch (unpub.) has suggested that this may be due to endomitosis or some similar process. There is, however, no evidence that polyploidy or other abnormal nuclear conditions are etiologically related to any tumorous process. Questions as to the mode of formation of these polyploid cells and of their possibly greater selection and division potential are still unanswered.

Physiology and Biochemistry

There has been little work done on the biochemistry of duplicating tumor tissues. Tsao and Whaley (1950) found that phosphorus^{32} was accumulated more vigorously by tumor tissues than by comparable normal mature tissues from the same plant. The concentrations of total phosphorus in tomato stem tumors was greater than in stem apices and much higher than in mature stem tissues. Klein (1952), in a study of the changes in phosphorus-containing compounds in tomato tumors, found that within five days after inoculation the total phosphorus was significantly increased in the young tumor. This augmentation in phosphorus was due to increases in orthophosphate and, particularly, in acid-soluble organic phosphorus. The latter fraction consisted of nucleotides, sugar-phosphate esters, and the phosphorus-containing coenzymes. Within 14 days after inoculation, the total phosphorus in the tumors was twice that of mature control tissues and over half of the increased amount was in the acid-soluble organic fraction. There is some evidence (Klein, unpub.) that a large fraction of this was present as adenosine triphosphate. These data show that the tumor is a highly active tissue system with strong oxidative phosphorylative capacities. Comparisons with meristem tissues of healthy plants have not been made.

Although no significant changes were noted in the ribonucleic acid (RNA) levels during the duplication of bean or tomato tumors, the desoxyribonucleic acid levels rose during the Duplication Period, with consequent modification of the DNA/RNA ratio. In normal stem tissues of tomato this ratio was approximately unity, but it reached a value of almost five in the tumor by the end of the Duplication Period. Comparable changes occur in tumors on the broad bean (Klein, Rasch, and Swift, 1953). This increase in the DNA of the bean tumor tissues was due both to increases in the numbers of cells per unit weight of tissue and to increased percentages of polyploid cells in the tumor mass.

Both protein and soluble nitrogenous fractions increased in the tissues of tomato tumors during this period (Klein, 1952). This nitrogen apparently was mobilized from the rest of the plant. Lee (1952) was unable to find any qualitative differences in the amino acid composition of normal and tumorous tissues of grape grown in vitro. He reported that both soluble and protein nitrogen were higher in tumors than in normal tissues. Link et al. (1936, 1953) studied the growth behavior of tumor-bearing tomato plants grown under adequate and restricted supplies of nitrogen (Figs. 2, 3, 11, 12). They found that, although the de-

ficient plants were considerably smaller, and grew much slower than the plants receiving nitrogen, the tumors were almost as large as those borne on the larger plants. Relative to the weight and size of the entire plant, tumors on the deficient plants were several-fold larger.

These reports on the accumulation of metabolites and intermediates suggest that to some extent the growth rates of tumor cells are independent of the growth rates of the host. It appears that dominance for growth potential and for the mobilization of nutrients passes from the apical growing point of the host to the tumor (Figures 2, 3, 11, 12). In cases of severe injury to the host, the tumor may attain such an ascendency over the growing points that the apex of the plant may die although the tumor persists (Levine, 1920; Link et al., 1953) (Fig. 12). Given a minimal concentration of metabolites, tumor cells may grow in vivo at rates only slightly affected by the nutrition, or the growth behavior of the host. To date, no auxin-induced neoplasm has shown these characteristics.

It has been postulated (Link and Goddard, 1951; Klein and Klein, 1953) on the basis of growth and metabolic studies that tumor tissues are not physiological analogs of normal meristematic tissues. Differences between these two types of dividing tissue may be both quantitative and qualitative, involving levels of inhibitors necessary to suppress development (substrate and cofactor affinities), differences in physiological behavior, and modifications in morphological responses. To date, this assumption has not been subjected to rigorous testing.

White (1945b) examined the respiratory behavior of healthy tissues of sunflower and tobacco stems, and of tumor tissues of these plants in vivo or in vitro. He found relatively slight differences in the rates of respiration and fermentation, and some modification in the respiratory quotient. In general, the tumor tissues grown in vivo or in vitro respired at lower rates than the healthy tissues. On the other hand, Klein (1952) and Klein and Klein (1953) demonstrated that tumor tissues of tomato in vivo, during the Duplication Period, showed higher rates of respiration and fermentation than healthy stem tissues. The respiratory quotient was elevated. If gas exchange was calculated on the basis of the amount of DNA in the tissues (assuming reasonably constant DNA concentrations per cell) the respiration was about forty per cent greater than for normal tissues. One must conclude that metabolic comparisons between tissues in vitro and those grown in the host must be referred to some common base, preferably an individual cell. Lioret (1953a, b, c) has made respiration studies on normal and tumor tissues of salsify grown in vitro. On a weight basis, the tumor tissues respired at a rate considerably higher than the normal tissue. He also noted that the longer the tissue was in culture, the lower was the respiratory intensity. This could be due either to the accumulation of non-metabolic material in the tumor masses or to the accumulation of toxic products of metabolism in the culture tubes.

FIG. 12. LOW-NITROGEN INOCULATED TOMATO PLANTS

Lower leaves died progressively and were shed prematurely, as tumor grew. Uppermost leaves, together with the apical portion of the plants, have died prematurely, with absence of abscission due to death of the apex of the axis, while tumor still is growing at expense of the rest of the nitrogen-starved plant. Reproduced from Link, et al., 1953.

The isolation of sterile crown-gall tumor tissues from secondary tumors, from tumors sterilized by heat treatments, or from primary tumors made it possible for investigators to study the physiological

and biochemical characteristics of the tissues in vitro, free from the influences of the host, the bacteria, and the uncontrolled environment. Similar studies have been made using tissues from *Rumex* plants infected with the wound-tumor virus (Burkholder and Nickell, 1949) and with tissues derived from hybrid tobacco plants (White, 1951a). The general conditions of culture have been reported by Hildebrandt et al. (1945, 1946a, b) for tumor tissues of sunflower and hybrid tobacco tissues. In the main, there are only small differences in the requirements of these tissues from different hosts for satisfactory growth in vitro.

The carbon requirements of several of these tumor tissues were investigated by Hildebrandt and Riker (1945, 1949, 1952, 1953). Hexoses and disaccharides appeared to be the most satisfactory sources of carbon; polysaccharides were poorly utilized, if at all. Organic acids were usually not utilized in the absence of sucrose (Hildebrandt, 1950), and alcohols were poor carbon sources (Hildebrandt and Riker, 1947a). The nitrogen requirements of crown-gall tissues were examined by Riker and Gutsche (1948), Frank et al. (1951), and Eberts and Riker (1952, 1954). Nitrate or urea were the best sources of nitrogen, peptone and other complex mixtures were fair sources, but most of the amino acids did not support growth. Henderson, Durrell, and Bonner (1952) reported that casein hydrolysate permitted excellent growth of sunflower tumor tissue. Glutamic and aspartic acids were tested in a wide range of concentrations and appeared to be fair to good sources of nitrogen. In several cases a bimodal concentration-response curve was observed, and in all cases linear growth response occurred only in a limited range.

In general, correlations based on the data for the nutritional requirements of tumorous tissues in vitro are unsatisfactory. White (1951a, b) discussed this problem and concluded that the nutritional differences among the various tissues tested are small and of doubtful significance. DeRopp (1951c), on the other hand, concluded that the nutritional behavior showed that crown-gall tumor tissues have simpler nutrient requirements than do the normal tissues from which they are derived. He postulated that tumor tissues possess a more complete enzyme system than normal tissues. These conclusions are not warranted by the limited studies reported to date. The failure of most investigators to run experiments on normal tissues, or on auxin-induced neoplastic tissues, parallel with those on tumor tissues, is a serious omission and one which precludes any direct comparison of requirements or metabolic pathways in the various types of tissue. Further, the ability of cells to utilize any given nitrogen or carbon compound is conditioned by the ability of the molecule to penetrate the cell. Penetration is, in turn, a function of the effective molecular size and affinity of the compound as well as of its degree of dissociation. The critical experiments necessary to elucidate these important problems have not been performed.

Effects of Various Chemical and Physical Agents

The literature on crown-gall tumors contains numerous reports on the effects of chemicals and of physical agents on the growth of tumors in vivo and in vitro. Some of these data may be pertinent to our understanding of the etiology of the changes in tumor-cells, although others are either without adequate explanation or have not been confirmed. In any case, they are of sufficient potential importance to review. Experiments of this type were motivated by economic considerations (cf. Riker and Berge, 1935; Ark, 1941), since crown-gall has been a serious disease on some cultivated plants. In many of these studies, the work was based on attempts to kill or to inactivate the "causal" organism. They were, of course, only successful when the treatments were made at the time of wounding. In other instances, the treatments were such that the host or the tumor was affected. The study of the effects of antibiotics are examples of this point.

A number of antibiotics have been tested for their ability to induce the regression of tumors. Brown and Boyle (1949a, b; 1945a, b) used crude preparations of penicillin to induce necrosis of the tumors on several plants of horticultural value. Hampton (1948) noted that low concentrations (20 to 50 units/ml.) of either streptomycin or penicillin caused the tumors to dry up without affecting normal tissues or morphologically normal shoots growing out of the tumor mass. Similar data have been reported by Klenkowski (1948), Darpoux (1950), and Pieri (1953). Brown (1948) noted the selective destruction of the nuclei of tumorous cells following application of crude penicillin to the surface of the tumor. Rebert and Havas (1951) have also reported that crown-gall could be cured by applications of penitaline, an

antibiotic obtained from *Penicillium italicum*. These reports have not been confirmed by other workers. DeRopp (1948c, 1949a), Klein and Klein (unpub.), and Dye and coworkers (1950a, b, 1951, 1952) examined the effects of a number of crude and purified antibiotics for tumoristatic activity with generally negative results. DeRopp (1949a) observed a stimulation of the growth of *Vinca* and of sunflower tumor tissues in vitro in the presence of a wide range of penicillin concentrations, and only slight inhibitions of growth by 50 to 500 gamma/ml. of streptomycin. These concentrations were far in excess of those used by Brown and Boyle or by Hampton. Dye (1950a, b) also obtained negative results with penicillin, streptomycin, streptothrycin, and actinomycin. Similarly, Stapp (1951) failed to inhibit tumor development with purified penicillin G. There is, at present, no explanation for this divergence of results. Recent modifications in the microbiological and isolation procedures used for the commercial production of antibiotics, with attendant modification in the purity and composition of the products obtained, may be the explanation. Proceeding along these lines, Stapp (1951) tested several of the byproducts of penicillin manufacture as well as other fungal products, but with negative results. It is clear that any cures effected by antibiotics are not due to bacteriostasis but may involve specific actions of the test agent on the metabolism of the tumor cells (cf. Manil, 1953).

Havas (1935, 1939a, b) introduced animal hormones into plants which bore stem tumors. Estrogens increased the weight of the tumors, as did thyroid and anterior pituitary hormones. The thymus hormones were inhibitory. Stapp (1937) was unable to obtain positive results with sex hormones. Ark (1937) and Paluch (1938) injected papain and pepsin into geranium tumors, with mixed results. Paluch concluded that proteolytic enzymes were not always effective in the treatment of crown-gall. Ark (1937) reported that soft-rot bacteria, producing pectic enzymes, killed tumor cells without affecting the host tissues. Havas (1936) applied an aqueous suspension of crushed mistletoe berries to tumors of tomato and castor bean and reported that the tumors were severely inhibited. Tumor inhibition occurred also when the extracts were absorbed by the host prior to inoculation. Podophyllin also induced regression of tumors (Havas, 1948).

Havas (1937), Solacolu and Constantinesco (1939), Brown (1939, 1942), Dermen and Brown (1942a, b), and Dye et al. (1950) all reported that colchicine was capable of arresting tumor-cell duplication. Stapp (1944) could not repeat these findings, but he used apple seedlings and *Datura* plants, and the other workers had used tomato, geranium, and castor bean plants. Solacolu and Constantinesco (1939) found that colchicine killed the tumors by suberizing the tissues adjacent to normal tissue of the host, thus interrupting continuity with the vascular strands. Brown (1942) stated that it acted by inducing excessive polyploidy in tumor cells which then became incapable of division. Since polyploidy is not unusual in tumor tissues (Klein, Rasch, and Swift, 1953), Brown's hypothesis is unsatisfactory. It would be more reasonable to assume that colchicine prevents division of the cell by preventing separation of the chromosomes at metaphase. Whether this compound acts specifically on tumors as contrasted with other rapidly dividing tissues is questionable.

Vitamins have also been supplied to tumors in vivo and in vitro. Ascorbic acid was reported to stimulate tumor development in tomato (Havas, 1935), and vitamin K had either little effect (Havas, 1948), or reduced the growth of the tumors (Havas, 1951). Havas (1939) reported that vitamins A and D would increase the percentage of tumors formed on *Opuntia* when applied to the site of inoculation. This experiment, however, was not sufficiently controlled to be of value. Henry, Riker, and Duggar (1943) have shown that thiamine was present in high concentration in young tumors and suggested that it may be used during growth. Thiamine and several B-complex vitamins are routinely used in tissue culture studies with tumor tissues. DeCapite (1952) demonstrated that para-aminobenzoic acid was required by crown-gall tumor tissues of salsify, and Hildebrandt, Riker, and Duggar (1945) found that pantothenic acid was needed for optimal growth of several tissues of crown-gall origin. Bourequet (1952) has recently observed that mercaptoethylamine, the reactive portion of the coenzyme A molecule, stimulated the growth of salsify tumor tissues in vitro. These fragmentary reports serve to indicate the necessity for careful comparative studies of the growth factor requirements of tissues in vitro. The use of antimetabolities of the vitamins would be an excellent starting point.

In recent years there has been some interest in

the effects of naturally occurring growth substances on the proliferation of tumor tissues. Duhamet (1950, 1951a, b) reported that coconut milk was capable of enhancing the growth of crown-gall tissues, in some cases up to 500 times as compared with growth on synthetic media. Duhamet (1953) found that very small fragments of salsify crown-gall tissue (0.5 to 2.0 mg.) would not grow unless supplemented with coconut milk. He postulated that low concentrations of "division substances" in the small fragments were limiting for cell division and that the coconut milk contained these materials. Demetriades and Nitsch (1953) found that normal tissues were more sensitive to coconut milk than were the crown-gall tissues of these plants. Paris and Duhamet (1953) prepared a synthetic coconut milk from the reported concentrations of amino acids and vitamins in the natural product and found that this mixture was effective for salsify crown-gall tissues. Henderson, Durrell, and Bonner (1952) did not obtain similar results with tumor tissues of sunflower, and Braun (1953a) could not stimulate *Vinca* tumor tissues with coconut milk. Gautheret (1952) indicated that the growth of many tissues, although stimulated by coconut milk, was rather abnormal and that many tissues so treated did not survive transplantation. This point has not been checked experimentally with tumor tissues.

Nitsch (1951) grew tumor tissues of tobacco and cactus in tomato juice and found that both tissues were stimulated up to four times over the control. At concentrations above 25 per cent tomato juice, the tissues were slightly inhibited. Demetriades and Nitsch (1953) made a comparative study of the effects of tomato juice on normal and tumorous tissues of Virginia creeper and salsify. The salsify tissues were inhibited by all concentrations of the juice, although both Virginia creeper tissues were stimulated. In both species the normal tissues were more sensitive. Kovoor (1953a, b, c) has found that the juice of white grapes and extracts of certain tropical fruits stimulated the growth of salsify tumor tissues. A liquid taken from the calyx of *Spadothea* flowers was inhibitory to tumor tissues but stimulated normal tissues. Hildebrandt, Riker and Duggar (1946a) found that extracts of tumor tissues, yeast extract, and metabolic products of crown-gall bacteria had slight, if any, stimulatory effects when added to synthetic medium used to culture crown-gall tissues. It is of general interest that most of the data on the stimulation of tumor tissues in vitro by natural products were obtained in the study of tobacco and salsify tissues. These, it will be remembered, are the only ones which showed significant stimulation by growth substances. When normal tissues were used for comparative study, it was found that they were more sensitive than the tumor tissues. One may ask whether the enhanced growth of tissues in these supplemented media may not be due to the presence of auxin-like fractions of the juices and extracts (but cf. Lioret, 1952b). Neutral and basic fractions with biological auxin action were not removed in the preparation of these test substances even when IAA could be presumed to be absent. This does not imply the absence of substances with important biological functions in these materials of natural origin. It merely suggests that the use of tumor tissue for bioassay is unsatisfactory for this purpose.

In 1939, Nabelek placed sunflower seedlings under a bell jar with a ripe apple. Typical epinastic responses were noted, and the growth of the seedlings was inhibited. Tumors on these seedlings, however, grew better than on control plants. Stapp (1943) repeated this work, using geranium plants, with identical results. The responsible volatile substance most likely is ethylene, but this possibility has not been tested.

Some attention has been paid to the specific inhibition of tumor-cell duplication by substances which interfere with nucleic acid metabolism. In contrast to a negative report by Verona and Luchetti (1937), Dimond, Stoddard, and Rich (1951) reported that several dyes which can combine with nucleic acids, notably aniline blue and malachite green, inhibited tumor growth in vivo. Demetriades (1953a) confirmed the finding of inhibition with aniline blue and showed that low concentrations of this dye would inhibit the duplication of grape tumor tissues in vitro but did not affect the growth of the normal tissues of grape. DeRopp (1949b) reported that four antimetabolites of folic acid prevented tumor development on carrot, apparently by killing the tumor cells. Normal tissues were also inhibited. The inhibition could be partially reversed by concomitant additions of folic acid. Manil and Straszewski (1952) also inhibited tumor growth in tomato with aminopterin, one of the anti-folic compounds. DeRopp (1951b, 1954) inhibited the development of Paris Daisy stem tumors with antimetabolites of purine and pyrimidine bases,

but he was unable to reverse the inhibition with additions of the normal base.

In view of the intensive study of the mineral nutrition of plants, surprisingly little work has been done on the effects of various ions on tumor growth in vivo or in vitro. Rives (1932) reported that plants grown without potassium formed larger tumors than those in complete nutrient solutions. Verona (1938) and Verona and Celastri (1938) confirmed this report and stated that calcium and magnesium ions were even more effective than potassium in suppressing tumor development. Potassium nitrate was more effective than the chloride. Kent (1941) found that lithium ions also suppressed tumor development. Sulfate, sulfide, or nitrate were effectively inhibitory anions (Verona, 1938, 1945; Florenzano, 1946). Aluminum ions (Verona and Celastri, 1938, 1939) and copper ions (Stapp and Bortels, 1933) had no effect on tumor development, although they were toxic to the host. Mercury, cadmium, strontium, zinc, lead, and barium stimulated the growth of the tumors (Sempio, 1935). Cobalt (Sempio, 1935), germanium (Gosset et al. 1934), and iron (Marcelli, 1950) specifically prevented the growth of tumors or caused necrosis of the tumor mass. Heller (1952) has studied the effects of many ions on tumor growth in vitro. These studies, incomplete as they are, suggest that the tumors possess anomalous biochemical patterns as compared with normal tissues of the same host. Only future research can determine the extent and direction of these metabolic modifications.

Two physical systems which have been reported to affect tumor growth are worth mentioning. Magrou and Manigault (1946, 1947, 1948) have reported that when freshly inoculated geranium plants were exposed to a directional, elevated magnetic field, tumor development was suppressed. Growing tumors were not affected to any large extent, and the growth and form of the bacteria was unaltered. Stapp (1953) was unable to confirm these observations. Gosset et al. (1924) reported that subjecting tumor-bearing plants to a "radio-cellulo-oscillator" (which produces waves two meters long with a frequency of 150 million per second) suppressed the development of the tumors. This report has not been confirmed.

There has been very little work on the edaphic factors which affect tumor growth. Levine (1921b) reported that certain soil factors, particularly the availability of nutrients, determine the vigor of the host and, consequently, the development of the tumors on the plant. Link et al. (1953) have shown that limiting amounts of nitrate-nitrogen have little effect on the growth of tumors borne on the plants, the tumors taking their nitrogen from the host (Figs. 2, 3, 11, 12). Riker and Keitt (1926), Riker, Hildebrand, and Keitt (1930), and Riker and Hildebrand (1934) found that apple twigs infected with crown-gall bacteria in the late spring usually show no tumor formation until the following spring. Tumor initiation and growth apparently are functions of the growth capacity of the host tissues (C. O. Smith, 1913; Stapp and Pfeil, 1939). Similar conclusions were reached by DeRopp (1951c), working with hypocotyls of sunflower.

Role of Growth Substances

The work discussed so far has indicated that during the Duplication Period cells of the tumor mass possess the capacity for autonomous, often rapid, proliferation. The biochemical basis for this proliferative capacity is a question of considerable importance. With the discovery of plant growth substances and the investigation of the effects of these substances on plant cells, a number of workers turned their attention to the possible role of growth substances in the multiplication of tumor cells. Blumenthal and Hirschfeld (1922), Siegler (1928), Brown and Gardner (1936, 1937), Link et al. (1937), and Locke, Riker, and Duggar (1938) observed that the presence of a crown-gall tumor on a plant was associated with many host responses which could also be produced by applications of indole-acetic acid (IAA) to the stem.

Link, Wilcox, and Link (1937), Locke, Riker, and Duggar (1938), DeRopp (1947b), and Appler (1951) reported epinasty of petioles (see Figs. 2, 3), suppression of lateral shoot development, stimulation of root production (see Figs. 3, 5), suppression of leaf enlargement, and cambial stimulation, all now ascribable to growth substances emanating from the tumor. That these responses are not due to any growth substances synthesized by the bacteria in situ was later demonstrated by the finding that they occurred in plants bearing sterile tumors (DeRopp, 1947b, 1948b; Camus and Gautheret, 1948a, b, c). Link and Eggers (1941) reported that the tumors themselves are high in an auxin which appears to be solely IAA (Locke, Riker, and Duggar, 1939a).

Sterile tumor tissues in vitro also synthesize large amounts of IAA (Kulescha and Gautheret, 1948; Kulescha, 1949) as well as indole acetonitrile and, possibly, indole pyruvic acid (Bitancourt et al., 1954). In some instances there were up to fifty times more auxin in tumor tissues than in normal tissues in vitro (Kulescha, 1950).

Locke, Riker, and Duggar (1938) tested agar blocks for their auxinic activity by the coleoptile method after allowing diffusion of growth substances into agar from inoculated and non-inoculated axes of tomato seedlings. They found that inoculated plants contained more auxin than did non-inoculated plants. They were unable to obtain auxinically active diffusates or active chloroform or alcohol extracts from mature tumor tissues.

Riker, Henry, and Duggar (1941), in spite of their own observations of the obvious effects in plants ascribable to excess levels of auxin in the tumors, reported that their bioassays failed to detect "significant" increases in IAA in tumors borne on tomato plants. This negative finding was obtained both when they calculated the concentrations of IAA on a total nitrogen basis and on a weight basis. They concluded that auxin played no role in tumor production. The failure of Locke et al. (1938) to obtain IAA by diffusion from old tumors is most probably due to the absence of any polar auxin gradient in tumor tissues which possess abnormal polarity relations (Link and Eggers, 1941). They found comparable amounts of auxin in tumors of either high-nitrogen or low-nitrogen tomato plants in which there was a several-fold difference in the nitrogen content of the tumors. It now appears to be well established that crown-gall tumor tissues, in vivo and in vitro, contain levels of growth substances several times higher than comparable normal tissue.

The biochemical basis for this hyperauxiny is not well understood. Link and Eggers (1943) studied the auxin synthesis of fresh and lyophilized tissues of tomato tumors in the presence of tryptophan. Crown-gall tumor tissues were considerably more active than normal stem tissues, presumably by possessing more, or more active, enzyme systems for this conversion. Bitancourt (1949) reported that normal sunflower stem tissues possess IAA-inactivating enzymes which are absent in crown-gall tissues of this host. This finding could not be confirmed by Henderson and Bonner (1952), who reported that sunflower tumor tissues not only possessed more active enzyme systems for the conversion of tryptophan to IAA, but that there were no IAA-inactivating enzymes present in either the normal or the tumor tissues. They also stated that normal tissues possessed inhibitors for IAA synthesis which are absent from the tumor tissues. This suggested that hyperauxiny of tumor tissues is not a result of decreased destruction of auxin (Bitancourt, 1949) but of uninhibited synthesis. Platt (1953) reported that tissues from normal grape stems contained higher levels of "auxin-sparing" phenols than did tissues of crown-gall origin and that auxin destruction proceeded at maximal rates in tumor tissues. Klein (unpub.) has found that auxin destruction occurred in both normal and crown-gall tissues of several hosts but was several times greater in tumor tissues. It is most likely that both mechanisms of regulation, destruction and synthesis, are going on in both normal and tumor tissues (DeRopp, 1954). The problem becomes one of determining the vector relations of the slopes to obtain a correct knowledge of the endogenous levels. The conflicting experimental findings reported to date, plus several very glaring technical errors in some of the published experiments, indicate the necessity for a reexamination of this problem.

Independent of the biochemical basis for hyperauxiny, its regular occurrence in tumors and the observed effects of auxin on plant tissues suggested that these growth substances may play an etiological role in the duplication of crown-gall tumor cells. The experimental demonstration of such a role, however, proved to be quite difficult. Additions of IAA or other growth substance to slices of tomato crown-gall tissues had only a suppressive effect on their respiration, and organic acids did not reverse this inhibition (Mitchell, Burris, and Riker, 1947; Eberts, Burris, and Riker, 1951). Lioret (1952a, 1953b), DeRopp (1947a), Morel (1948), Gautheret (1948), and Kulescha (1951) found that many tissue cultures of crown-gall origin did not require auxin in the medium and were, in fact, inhibited by even relatively low concentrations of IAA. Hildebrandt and Riker (1947b) did observe some stimulation of sunflower tumor tissues in vitro by low (10^{-11} g./l.) levels of auxin, but their observed increases in weight were of doubtful significance (cf. DeRopp, 1947a). Crown-gall tissues of tobacco were stimulated by naphthaleneacetic acid at concentrations as high as 10^{-5} g./l. and were not

inhibited by 10^{-3} g./l. (Hildebrandt, Riker, and Watertor, 1952). Tryptophan was inhibitory to these tissues. In general, concentrations of growth substances which inhibit tumor tissues are necessary for the continued proliferation of normal tissues in vitro. It is possible that the failure to enhance growth rates, respiration, or development of tumor tissues by additions of growth substances may be due to the presence of saturating or optimal concentrations of these materials formed within the tumor cells (auxin-autotrophy). Under these conditions even small amounts of added auxin could be sufficient to evoke inhibitory responses. Yet none of these reports nor any dealing with auxin content or synthesis has provided rigorous proof that auxin plays a specific role in the duplication of tumor cells.

Several other lines of research have presented pertinent information on this important point. Gautheret (1952a) reported that tissue cultures of artichoke tubers, which require IAA for growth, were inhibited by maleic hydrazide. At several levels of this reputed antiauxin, the suppressive effects were released by added auxin. Waggoner and Dimond (1953) reported that maleic hydrazide significantly reduced the size of tomato tumors in vivo and of carrot crown-galls in vitro. Manil and Straszewski (1952) and Klein and Klein (1952), on the other hand, found that concentrations of maleic hydrazide which reduced the vegetative growth or development of *Datura* or of tomato plants to half of control values had no effect on the respiration or the growth of tumors borne on these plants. Klein and Vogel (unpub.) failed to confirm the report of Waggoner and Dimond. Perhaps the clearest demonstration of the inhibiting effect of maleic hydrazide on tumor growth was provided by Kulescha (1953). Using tissue cultures of salsify crown-gall, she found that concentrations of 10^{-7} g./l. of maleic hydrazide significantly reduced the growth of the tumor tissues. In no instance was there any diminution in the concentrations of IAA in the inhibited tissues. This indicates that if maleic hydrazide is an antiauxin, it acts on the systems which use the IAA and not on the synthetic mechanisms. However, since these experiments involve several important differences in technique, a final decision on both the specific antiauxin activity of maleic hydrazide and its effect on tumor-cell duplication by interference with auxin metabolism await further study. If maleic hydrazide does act as an auxin antimetabolite, the concentrations necessary to inhibit divisions of tumorous cells appear to be considerably higher than those which will suppress the multiplication of normal cells. This may be a function of the heightened levels of auxin in tumor tissues or indicative of altered affinities of auxin for its active sites. Klein and Vogel (unpub.) have shown that 2,4,6-trichlorophenoxyacetic acid and IAA, each capable of inhibiting tumor-cell duplication in vitro, will antagonize the action of the other, resulting in a competitive and reversible antimetabolite–metabolite system. It was also shown that the affinities for the antimetabolite differed in normal and tumorous tissues. Roberts (1953) was able to suppress the epinastic responses associated with hyperauxiny of tomato tumors in vivo with a naturally occurring antiauxin. Of primary importance was the finding that the growth of the tumor was severely suppressed by this antiauxin. Struckmeyer and Roberts (1955) also demonstrated that this antiauxin inhibited the divisions of the tumor cells.

Recently studies have been made on the effects of ionizing radiations on auxin levels and on the growth of normal and tumorous tissues. Waggoner and Dimond (1952) found that doses of 3 to 5 Kr of x-rays suppressed tumor-cell duplication in tomato; the greater the dose, the more nearly irreversible was the inhibition. Above 6 Kr, no cell division occurred. This finding checks well with the earlier reports of Levin and Levine (1917a, b, 1918) and other workers (cf. Riker and Berge, 1935) on the suppressive effects of radiation on the growth of tumors in vivo. The finding that lower levels of radiation irreversibly inhibited tumor development is of immediate interest. Skoog (1935) and Gordon and coworkers (1950, 1953) found that auxin synthesis in higher plants was reversibly inhibited by low dose levels of radiation (0.25 to 1.0 Kr) and irreversibly inhibited by higher levels (1.5 to 2.0 Kr) without other observable injuries to the plant. Klein and Vogel (unpub.) exposed inoculated tomato plants at the beginning of the Duplication Period to 1.5 Kr of x-radiation and obtained almost complete inhibition of tumor development. This suppression of tumorous cell division could be completely reversed by applying IAA in lanolin to the bisected stump of the internode bearing the site of inoculation. Similar results were obtained with other ionizing radiations (gamma and fast neutrons) at comparable

ion densities. Contrary to the report of Waggoner and Dimond that the same mechanisms were involved in inhibitions of tumor-cell duplication at higher levels of radiation, Klein and Vogel were unable to reverse the inhibition induced by the higher levels of radiation by applying IAA. These radiation data, together with the antiauxin studies of Roberts, present the first unequivocal indication that growth substances synthesized by tumor cells are etiological agents in the duplication of these cells. Apparently the growth substances are synthesized by the cells which require them, i.e., crown-gall tumor cells are auxin-autotrophic.

Comparative studies of the development, physiological behavior, and morphological characteristics of crown-gall, normal, and of auxin-induced neoplastic tissues have shown that the tumor state is not solely a result of auxin autotrophy. Kulescha (1947a, b, 1951), Morel (1948), Gautheret (1952b), as well as other workers (cf. White, 1951b) have examined this problem by using tissue culture techniques. They noted that auxin-induced neoplastic tissues and normal tissues show a high degree of morphological regularity, may form roots and shoots in the tissues, and frequently develop well-oriented vascular elements in vitro. These activities are not usual characteristics of tumor tissues (cf. Demetriades, 1953). Friedeman and Francis (1942), using organ cultures of tomato roots, found that crown-gall tumors possess a somewhat different morphology than did neoplasms induced by known growth substances. Levine (1940), DeRopp (1951b), and Appler (1951) all demonstrated that there were several fundamental differences between auxin-induced neoplastic tissues and tissues of crown-gall origin. The former appeared to be sufficiently under the morphogenetic restraints of the host to form normal root and shoot primordia within the neoplastic mass, whereas the majority of crown-gall tumors usually show no organ differentiation. Even more important is the fact that the neoplastic tissues resulting from treatment with auxins were not autonomous but either ceased to grow or reverted to normal patterns soon after the removal of the auxin (cf. Solacula and Constantinesco, 1936). Crown-gall tumor tissues, on the other hand, generally retain the autonomous growth habit and do not revert to the normal pattern.

Polyploidy, which frequently exists in cells of crown-gall tumors of bean, does not seem to occur to as great an extent in auxin-induced tissue, nor were the DNA levels of auxin-stimulated tissues increased greatly over controls. Ribonucleic acid levels of auxin-induced neoplastic tissues were not different from those of control tissues but were elevated in tumor tissues (Klein, Rasch, and Swift, 1953). Link and Klein (1951) observed that the oxygen uptake rates of normal tomato stem tissues were mediated through three heavy-metal enzyme systems in approximately equal amounts. In tumor tissues of tomato in the Duplication Period (13 days old) as well as in mature tumor tissues (50 days old) the ratios of these systems were shifted far in favor of a copper-containing system. Auxin-induced neoplastic tissues, on the other hand, showed a shift in favor of iron-mediated systems. Braun and Naf (1954) and Klein (unpub.) have evidence that crown-gall tumor tissues from many host species contain biologically active growth substances which are not IAA and which are found only in tumor tissues. The findings reviewed in this section indicate that auxin plays a role in the causal complex of tumorous cell division, as it probably does in the division of normal cells. Undoubtedly, hereditary, internal environal factors other than auxin of the host, past history, and external environal factors also enter into these causal complexes. Discussion of the possible modes of action of auxin in these causal complexes is deferred until a later section.

Summary of the Duplication Period

During the growth stage of the life history of a tumor, not only does duplication of the tumor cells occur, but this is also the period of secondary tumor-cell transformation and the initiation stage in the life history of tumors which are secondary both as to locus and to the initiation by secondary transformation.

Tumor cells and their progeny divide rapidly during the Duplication Period of cellular change and behavior, giving rise to a mass of tumor cells. During this period their behavior is completely independent of the crown-gall bacteria. These cells are characterized by prominent nuclei, cytoplasmic basophilia, and thin walls. Several cytological modifications, including loss of chloroplasts, are evident. Divisions occur in all planes, and many daughter cells may be formed within the confines of the enlarged parent cell. Differentiation of tumor cells, whether of primary or of secondary

origin, does not occur during the Duplication Period.

Duplicating crown-gall tumor cells differ markedly from normal, callus, or non-tumorous neoplastic cells. Both in vivo and in vitro, crown-gall tumor cells are auxin-autotrophic, requiring no exogenous supply of growth substances. This auxin appears to be an etiological agent for the multiplication of these tumor cells, being specifically required for growth processes. In most, if not all cases, the tumor mass contains high levels of growth substances and may be the source of the auxins present in excess throughout the plant. Tumor tissues are autonomous in growth rate, their cells duplicating at rates differing markedly from those of the host and usually in excess of the rates characteristic of healthy tissues. Duplicating crown-gall cells are also autonomous in form, apparently not being greatly affected by the morphogenetic restraints and patterns imposed by host tissues on their normal cells. In vitro and in vivo, the tumor maintains its characteristic growth habit and generally does not differentiate into nor produce normal organs, as do callus tissues. The rates of respiration and fermentation of tumor cells differ from those of comparable normal tissues, and the levels of nitrogen- and phosphorus-containing compounds are elevated. In vitro, duplicating tumor cells have the ability to utilize a fairly wide range of carbon and nitrogen sources and are less dependent than are normal cells upon exogenous supplies of vitamins and other growth factors.

MATURATION STAGE OF A TUMOR

Organization and Differentiation Period

During the maturation stage of the life history of a tumor, cellular differentiation and organization of cells and tissues into a structurally complete tumor occurs (see Figs. 8–10). This stage is characterized by cellular organization and differentiation, which begins with the first histologically detectable differentiation of cells of the tumor mass. This mass consists of primary and secondary tumor cells, their derivatives, and occluded normal cells and their derivatives. In so far as the neoplasm consists of tissues which provide a habitat and supply nutrients for the bacteria, it is not only a tumor but also a kataplasmic gall, according to the classification of Küster (1915). If the bacteria disappear from tumors of primary origin, or are initially absent, as is the case of crown-galls of secondary origin, the mass may be considered merely a tumor.

Many workers have reported that crown-gall bacteria were more abundant near or at the surface of mature crown-gall tumors than within it (Magrou, 1926; Riker and Berge, 1935). The isolation of sterile crown-gall tissues from primary tumors of beet (Jensen, 1918), sunflower (DeRopp, 1947c) and other plants (Morel, 1948; DeRopp, 1951c) demonstrated that the numbers of crown-gall bacteria decrease as the tumor becomes older and larger and that the bacteria frequently disappear entirely (Siegler, 1929; DeRopp, 1951c). The explanation of these findings may be sought along two lines: first, that the development of tumor cells is a defense reaction against the bacteria (Levine, 1936; Gäumann, 1948); second, that physical conditions in tumor tissues are unfavorable for the continued survival of the bacteria. No convincing demonstration of antibody formation has been reported for crown-gall. In fact, Klein and Klein (1953) found that virulent crown-gall bacteria grew well in extracts of tumor tissues. The presence of large quantities of utilizable substrates in tumor tissues, and the availability of adequate supplies of minerals and water suggest that nutritional deficiencies are unlikely to be involved in any postulated defense reaction.

On the other hand, the decrease in the bacterial population may be related to the relative oxygen dependence of the tumor tissues and the bacteria. The crown-gall bacteria are obligatory aerobes, dying when the oxygen tension decreases although the tumor cells have well-developed fermentation mechanisms (White, 1945; Klein, 1952) and show good Pasteur effects (Neish and Hibbert, 1943a). On a dry-weight basis, tomato tissues respire at rates somewhat in excess of the bacteria (Klein and Klein, 1952). Soru (1931) and Riker, Pinckard, and Baldwin (1939) pointed out that crown-gall tumors in vivo raise the redox potential of the tissues. Since the diffusion of oxygen through tumor tissue is low, gas exchange becomes more difficult as the number of closely packed, hyperplastic cells increases. Under these potentially anaerobic conditions the bacteria cannot compete with the tumor cells for the available oxygen and have greatly reduced survival potentials (Hill and Mills, 1954). They will die out at the center of the tumor and will be found only at the periphery where oxygen is not so severely limiting. This

second hypothesis fits the facts well and precludes the necessity of postulating any defense mechanisms.

Structure and Morphology

In tumors of tomato stem tissues, cellular and tissue changes usually are showing organization and differentiation within 15 to 20 days after inoculation (Riker, 1923b; Buvat, 1945; Klein, 1952). As would be expected, this time varies with the species of host plant, the strain of bacteria used, and with the environmental conditions. Robinson and Walkden (1932) found that cellular alterations in the Paris Daisy were clearly evident within 15 days after inoculation. Klein, Rasch, and Swift (1953) and Rasch (unpub.) observed maturation of tumor cells of the broad bean within 9 days, and Noel (1946) and Magrou and Manigault (1948) reported the presence of lignified elements in geranium tumors within 16 days. In tumors which grow slowly, such as those on woody twigs and *Bryophyllum* stems, differentiation may not be histologically detectable for a month or more after inoculation.

The sequence of histological change in vivo is essentially the same for most tumors. The rates of division of tumor cells decrease sharply. Some of the small tumor cells begin to enlarge, their walls undergo characteristic secondary thickening, and differentiation of these cells becomes evident. Examination of mature crown-gall tumors shows a tissue system composed of small tumor cells, some giant cells, and many cells with thickenings and lignifications resembling those found in normal sclerids and tracheids (see Figs. 8–10). The rates of water flow through the stem are severely reduced by this vascular distortion (Melhus, Muncie, and Ho, 1924). In time, these lignified elements, often quite distorted during their formation, present such an intricate pattern that it is impossible to detect any common pattern of formation. They are all derived from tumor cells and are differentiated by pitting, secondary thickening, and lignification. The lignifications do not attain the same degree of differentiation as that observed in normal secondary differentiation of xylem cells. Nests of giant cells are seen, apparently derived by cell enlargement or by fusion of several tumor cells. They frequently are binucleate. Nevertheless, the bulk of most tumors is composed of small, thin-walled cells (Gautheret, 1947) which are very tightly packed (Flint, 1951) (see Figs. 8–10). Most workers agree that the tracheids and spirally thickened tubes are formed de novo from tumor cells (Cook, 1923; Banfield, 1935; Jones, 1947). Intrusive growth of lignified tumor cells into the stele of the host are generally held responsible for the disruption of the continuity of the normal vascular system. In many cases (Link et al., 1953), (Fig. 5), the tumor may actually split the stem. Many workers have reported de novo formation of centers of meristematic activity within the tumor (fig. 8). Magrou (1926, 1927) and Muller (1935) observed that "supernumary steles" were formed in old tumors of sunflower, tomato, and other plants. These are characterized by peripheral phloem and central xylem separated by a "generative zone." Intermedullary steles have also been seen, showing an inverted order with central phloem and peripheral xylem. Noel (1946), Jones (1947), and DeRopp (1951c) have observed this generative unit in tumors on several hosts. This ability of tumors to form vascular tissues may be related to the ability of the tumor to obtain some nutrients by direct connections with the vascular tissues of the host (McKeen, 1954a).

The gross morphology of a mature crown-gall tumor has been described many times. In general, a typical tumor is an irregularly globose mass with a more or less convoluted surface (see Figs. 1–3, 11, 12). It may, depending on the host and on other factors, range from the size of a pea to that of a basket-ball, although tumors of this large size are found infrequently. When young, many tumors are almost white (Fig. 1C), but they may darken and weather with the peripheral differentiation of a periderm. In certain hosts, usually woody perennials, the tumor may be quite woody—the so-called hard gall—but most tumors, especially those on herbaceous plants, remain succulent soft galls (Smith, 1911). Frequently, recognizable organs appear (Fig. 8 B) apparently originated within the tumor itself (Smith, 1927). Siegler (1928, 1929, 1930) and Brown (1929), as well as earlier investigators, (Smith, 1911), reported that roots arise within the tumor (Figs. 3, 5, 8). These tumors, some of them incited by variants of the crown-gall bacteria (Riker and Berge, 1935; Riker, Spoerl, and Gutsche, 1946; Riker and Hildebrandt, 1951), have been called woolly-knot galls (Siegler, 1929), hairy-root tumors, witches brooms, etc. Brown (1929) demonstrated that root formation within

tumor tissues was, to some extent, dependent on the host plant. Some species regularly form root-containing tumors; others never show this character. Certain strains of crown-gall bacteria, however, are ineffectual in inducing these structures, even in plants disposed to their formation (Braun, 1948).

More complex tumors have also been observed. Smith (1911, 1917) and Magnus (1915) reported that crown-gall tumors may contain tissues showing rather remarkable morphological similarities to normal structures of the host plant. Such tumors have been observed on a wide range of hosts (Levin and Levine, 1918; Oppenheimer, 1926). Küster (1926) described in some detail the form anomalies of leaflets on tomato and geranium tumor masses. He noted that they are never formed in callus tissues of these hosts but only on relatively mature crown-gall tumors. Magnus (1915) carefully described the types of structures found in relation to normal organs and termed these anomalies "Adventivorgane." Smith (1916b, 1921), using a term then current in oncology, called them embryomas or teratomas and maintained that they originated from groups of normal, pluripotent cells disrupted from their original site and stimulated into growth by the enlarging tumor mass. This concept has been accepted by Rack (1953), but Levine (1919, 1923b) rejected it and maintained that teratoma shoots arise de novo by differentiation of tumor cells and the subsequent organization of these cells into buds. He also questioned the concept of pluripotency and reported that teratomas did not result following the inoculation of crown-gall bacteria into the dormant leaf buds of *Bryophyllum*, which should have been composed of pluripotent cells. Smith (1921), in turn, criticized Levine's experiments and, using a different technique, obtained leafy teratomas following inoculation in *Bryophyllum* leaves. Following a sharp exchange of opinions, little work was done on this problem for about a deçade, although the protagonists continued to refer to their earlier work in subsequent papers (Smith, 1928; Levine, 1931, 1936). The derivation of these organized structures remained unknown.

In 1938, Locke, Riker, and Duggar reported that plant tissues inoculated with attenuated crown-gall bacteria at sites below mature tumors first developed shoots and leaves and then formed more typical tumor tissues. Klein and Klein (unpub.) found that inoculations into the apical meristems of tomato plants, with attendant disruption of normal internal structure, regularly resulted in the formation of teratomas. DeRopp (1947c) reported that cultures of tissues isolated from primary crown-gall tumors of sunflower gave rise to large masses of tissue containing both normal and tumor cells. On continued subculture of these teratomas, their tendency to produce differentiated tissue was lost. DeRopp (1951c) suggested that the more normal organs arose by the proliferation of normal, occluded cells and not from tumor cells.

This hypothesis, however, has not gone unopposed. Braun and Laskaris (1942) observed that adventitious shoots may arise subsequent to the development of tumor tissues. When Buvat (1945) inoculated tomato plants by scarring the stem with a scalpel bearing the bacteria (being careful to cut only into the outermost layers of the cortex), he found that leafy teratomas occasionally developed. Buvat reported that these arose by localized recrudescences of proliferation and by orientation of the mitoses of the tumor cells. This activity resulted in a small mass of oriented cells which were organized into buds and then formed shoots. They had no vascular connection with the stele of the host at any stage of shoot development, being dependent on the tumor for water and nutrients. Tatarinov (1937) and Kostoff and Kendall (1945) isolated tetraploid shoots from tetraploid tumors on tomato and suggested that, in view of the diploid nature of the normal tissues, the shoot must have been derived from tumor tissues. Lewis (1951), however, has pointed out that callus tissues on bisected stems of tomato normally regenerate a small percentage of polyploid shoots. Braun (1948) inoculated the surface of bisected stems of leaf blades of *Kalanchöe* plants with crown-gall bacteria and was able to demonstrate that the tumor developed first and that the morphologically complex structures were of secondary origin. He noted that the tumor originated from cells below the surface of the cut where the injured surface cells had died. Since plant cells are rigidly held in place by their cemented cell walls, the expanding tumor mass was unlikely to contain occluded normal cells. Histological studies of leafy teratomas showed that the tumor cells near the periphery of the tumor, and hence farthest removed from the point of origin of the tumor mass, were the progenitors of the buds and shoots. These findings were corroborated

by Braun (1951a, b) using tobacco plants, and by Klein (1954), using tomato plants. Thus, there is little doubt that both modes of derivation of teratoma shoots are possible, viz., from normal cells occluded in the tumor mass, and from tumor cells themselves. To some extent, both Smith and Levine were correct.

The teratomatous shoots derived from the tumor cells are of particular interest. Hampton (1948) reported that they are unaffected by concentrations of antibiotics which killed crown-gall cells. Braun (1948) showed that the more abnormal of these structures on *Kalanchöe* teratoma tumors were, like true crown-gall tissues, insensitive to any further stimulation by crown-gall bacteria. The more normal-appearing organs, on the other hand, occasionally responded to inoculation by the formation of undifferentiated crown-gall tumors. Some *Kalanchöe* teratomas gave rise to plantlets ranging in appearance from those which were almost undifferentiated, bulblike processes, to plantlets morphologically identical to those normally found in the leaf notches of these plants. In most cases, these plantlets failed to form roots when excised from the teratoma and did not develop into normal plants. When grown in vitro, with or without auxin in the medium, they usually dedifferentiated into a mass of slow-growing tumor tissues, the organized plantlets being engulfed in the tumor mass. Other tissue cultures produced a sterile, callus-like tissue at the base of the plantlet, the leaves remaining normal in appearance. A few of the teratoma plantlets, however, developed into completely normal *Kalanchöe* plants. These results indicated that on histological and morphological grounds, the teratomatous shoots can be placed in a series ranging from shoots which unquestionably are still tumorous to those which appear to be quite normal. If the abnormal shoots were derived from normal cells, removal of these from the influence of the tumor should have permitted their reversion to completely normal tissues. That this did not occur in the majority of trials (Braun, 1951b) is additional presumptive evidence of their tumorous origin. Assuming this to be the case, the formation of these teratoma shoots may most reasonably be explained on the basis of a more or less complete recovery of tumor cells from the stimuli which initially induced their tumorous character and by the subsequent organization of these recovered cells into structures which follow the morphogenetic patterns of the plant from which the cells were derived. This hypothesis is supported by the findings of the histological development of the shoots, as reported by Buvat (1945) and Braun (1948).

The recovery of tumor cells has recently been effected experimentally (Braun, 1951b, c). Morphologically abnormal tumorous shoots of tobacco, but not undifferentiated tumor tissues (Lance and Gautheret, 1952), were removed from the tumor in vivo and were grafted to healthy tobacco plants. The grafts took well, forming tumors with numerous shoots which were, in turn, grafted into other healthy hosts. By progressively selecting the more normal-appearing shoots for graft transfer, the grafts became more and more normal. Eventually, they flowered and set seed. Teratoma-like masses of hybrid tobacco tissues did not show this type of response (Braun, 1954). Tissue cultures of tissues of the teratoma taken at intervals during the recovery period showed that as they became more normal, their capacity for unlimited growth in vitro, a characteristic of tumor tissues, decreased. When, finally, the fragments isolated from normal-appearing tobacco tissue grafts were cultured in vitro, they grew as poorly as do healthy tobacco tissues. The normal polarity of the tissues—basal root formation and apical leaf formation—was gradually restored. The observed histological changes accompanying recovery followed the same pattern as did the morphological and growth potential sequences. Recovery appears to have been complete.

In 1952, Braun (1952b) advanced the hypothesis that the internal agents which keep cells in the tumorous state may be self-duplicating cytoplasmic entities. In support of this hypothesis he turned to analogous situations in other fields of cellular biology. Several investigators, using biological systems as different as the kappa infection of *Paramecium* and virus-infected shoots of sugar cane (Kunkel, 1924), had shown that self-duplicating cytoplasmic entities can be diluted out of cells when the rates of multiplication of the cells are in excess of the replication rates of the cytoplasmic agents. Braun, accordingly, assumed that following the grafting of teratoma shoots of tumors into healthy plants, the rapid division of the cells of the graft had outstripped the ability of the cytoplasmic entities to maintain a titer sufficiently great to keep the cells tumorous. As the number of these entities progressively

decreased per tumor cell, the cells showed increasingly normal characteristics and finally became freed of the tumorous condition. The results of these experiments present the best evidence to date that the agents which maintain cells in the tumorous state are related to cytoplasmic particles.

Physiology and Biochemistry of Tumors

Before discussing those studies which bear on the physiology and biochemistry of maturing and mature crown-gall tumor tissues, it is of value to examine briefly the rationale of those investigations. Analyses of constituents and activities of tumor tissues have been carried out to obtain information on the metabolism of the tissues with the hope that there might become evident a biochemical basis for the observed tumorous behavior of the tissue. Prior to the last decade, most workers proceeded on the hypothesis that all crown-gall tumor tissues are physiologically idential, irrespective of their developmental or etiological "age." Thus many workers failed to report even the chronological age of the tissues they studied, and very few gave any information about the stage of tumor development. For this reason, their data are subject to question, and conflicting reports were inevitable.

An excellent example of the difficulties besetting any comparative biochemical investigation of tumor constituents and activities is encountered in the determination of the percentage dry weight of the tissues. Klein and Keyssner (1932a) and Muller (1935) reported that this value for tumors of tomato stems five to eight weeks after inoculation was 30 per cent higher than that for "control segments" of the same stem. Nagy and coworkers (1937, 1938) found that greenhouse-grown tomato plants, bearing six-week-old tumors, had the same percentage dry weight as control, healthy stems, although field-grown tomato plants bore tumors which had a considerably lower percentage dry weight. Link and Eggers (1941) found the same percentage dry weight in control and inoculated tomato hypocotyls from the twentieth to the twenty-ninth day after inoculation. Klein (1952) reported the percentage dry weights of control stem segments and tumors of other stems from the time of inoculation until necrosis of the tumor. He found that the values were identical until the end of the Duplication Period. After this time the values in the control tissues continued to rise while those of the tumor leveled off. Link et al. (1953) could not check the findings of Klein when the plants were grown in nutrient-sand cultures instead of soil. It is clear that even this presumably simple determination varies with age, growing conditions, stage of tumor development, and the tissues used for comparison. The problem of standardization for comparative biochemical studies becomes more difficult with increasing complexity of the character or process under examination. Nevertheless, when the available data are examined critically, certain general trends become evident.

This section on the physiology and biochemistry of crown-gall tissues will examine the data for (1) a representative herbaceous stem, that of the tomato plant, (2) a representative storage organ, the root of the sugar beet, and for their respective tumors. These have been chosen because of the large amount of information available relative to them as well as because of the considerable differences between the organs and tissues of tomato and beet.

Carbon metabolism. Quantitative determinations of the carbohydrate constituents of sugar-beet tumors (Strohmer and Stift, 1892; Neish and Hibbert, 1940) and of tomato stem tumors (Nagy et al., 1938; Stapp and Pfeil, 1939) showed that free sugars are highest in healthy tissues and lowest in tumor tissues, with mature non-tumorous tissues of tumor-bearing organs containing either the same amounts as the tumors or slightly more (Berthelot and Amoureux, 1936b). Starch was highest in the tumors of either host. Kostoff (1933) noted accumulations of starch within the tumor cells of sugar beets. Cellulose, pectins, and other non-utilizable carbohydrates showed few significant trends, but tended to be in slightly higher concentrations in beet tumors and in slightly lower amounts in tumors of tomato. Neish and Hibbert (1940) and DeRopp (1950a) observed that when tumors form on storage organs, they show a remarkable ability to utilize the food materials stored in those organs. The high level of carbon utilization in tumor tissues suggests that the carbon chains are being used for synthesis of protein as well as for the formation of cell-wall materials (Neish and Hibbert, 1940).

One major pathway for carbohydrate utilization in plant tissues is through oxidation of organic acids metabolized via a tricarboxylic acid cycle. Link, Klein, and Barron (1952) have shown that

this cycle is the main oxidation route for carbohydrates in normal stems of tomato. Berridge (1930) and Stapp and Pfeil (1939) reported that the pH of tomato tumor tissues was more alkaline than that of normal stem tissues, and Klein and Keyssner (1932) found more ether-soluble, titratable acidity in those tumors. Similar findings have been made for sugar beets (Brown and Quirk, 1929; Stapp and Pfeil, 1939). Since the ash content of tomato tumors (Klein and Keyssner, 1932b; Nagy et al., 1938; Stapp and Pfeil, 1939) and of beet tumors (Strohmer and Stift, 1892; Berthelot and Amoureux, 1936b) is higher than in normal tissues, it is possible that organic acids formed from carbohydrates in the tricarboxylic acid cycle occur as their salts. Further evidence of the existence of an organic acid metabolism in tumors of tomato stems was provided by Eberts, Burris, and Riker (1955). They reported that additions of citrate, malate, succinate, etc., significantly increased the rates of oxygen uptake of washed slices of tumor tissues. Neish and Hibbert (1943a) studied the utilization of sugar and the carbon balance of slices of beet tumors and of non-tumorous tissues from the same specimen. Oxalic, malic, and citric acids present in the tumor tissues were metabolized in a dynamic equilibrium but were formed in excess of utilization by the "normal" tissues. Aerobically, reducing sugars were oxidized rapidly by tumor tissues, but most of the carbon apparently went into compounds not analyzed, viz., cell wall materials, proteins, etc. In the "normal" tissues, the formation of carbon dioxide and organic acids accounted for most of the carbon utilized and little specific synthesis occurred. Klein (1952) and Klein and Klein (1953) observed that the respiratory quotient of mature tumor tissues of tomato was significantly above the control value of unity. This increase may reflect the oxidation of compounds such as organic acids, or allied substances, which are in a higher state of oxidation than are reducing sugars. Muller (1935), however, had reported respiratory quotient values below unity for tomato tumors.

Almost nothing is known about the lipid metabolism of crown-gall tissues. Ether-extractable material is slightly greater in beet tumors than in healthy tissues (Nagy et al., 1937, 1938; Neish and Hibbert, 1940), and about the same in tomato tumors (Nagy et al., 1938). Klein (1952) observed no consistent trends in the phospholipid concentrations of tumor tissues, but there were slight increases in phospholipid-phosphorus during the maturation phase of tumor development.

Nitrogen metabolism. The most marked difference in chemical constituents of normal and tumor tissues are found for the nitrogen fractions. In beet, these differences were first noted by Strohmer and Stift (1892). Berthelot and Amoureux (1936b), Nagy et al. (1938), and Stapp and Pfeil (1939) found that the total nitrogen of the beet tumor tissues was about three times that of comparable healthy tissues, the bulk of this excess being present as protein. A more complete nitrogen distribution study was made by Neish and Hibbert (1943b), using "normal" tissues of the tumorous beet for comparative purposes. Over half of the protein of the tumors was water- and alkali-soluble, although over three-fourths of the protein of the non-tumorous tissues was insoluble. Neish and Hibbert (1943b) studied the aerobic and anaerobic nitrogen metabolism of slices of these beet tissues, ammonium sulfate being used as the nitrogen source. Tumor tissues showed greater protein synthesis, via amide formation, than the non-tumorous tissues. Under anaerobic conditions, protein was not synthesized by either type of tissue, although the ammonium ion was still fixed as amide. The carbon chains for this amide came from keto acids formed by the oxidation of malic and citric acids.

The picture is quite similar in tomato stem tumors, nitrogen being high in the tumor, the bulk of it present as protein (Klein and Keyssner, 1932a; Nagy et al., 1938). Link and Goddard (1951) found that tissues contiguous to tumors of tomato were usually higher in nitrogen than tissues of healthy control plants, the differences being most marked in plants grown under nitrogen-deficient conditions. Klein (1952) observed a rapid synthesis of protein concomitant with smaller increases in soluble nitrogen in mature tumors of tomato. This increased rate of synthesis occurred at a time when the tumor was in transition from the Growth Stage to the Maturation Stage. This suggests that maturing tumor cells accumulate much of their nitrogen as protein. Since alcohol-soluble nitrogen also accumulated in the tumor at this time, protein synthesis could not have occurred solely at the expense of the available amino acids and amides; nitrogen from the whole plant apparently was mobilized into the tumor. This point will be considered later in

relation to the base to be used for the calculations of various biochemical activities of the tumor tissues.

Phosphorus metabolism. Stapp and Pfeil (1939), Tsao and Whaley (1950), Manigault and Jussier (1951, 1952), Klein (1952), and Manigault (1953) all have reported that the total phosphorus of tumor tissues was considerably higher than that of healthy tissues. Phosphatase was also very active in stem tumors (Manigault and Jussier, 1952). Klein (1952) found that the total phosphorus content of the cells was highest at the end of their Duplication Period and declined steadily during their Organization and Differentiation Period. The bulk of this phosphorus was present in an acid-soluble organic fraction and as inorganic phosphate. The DNA-phosphorus level in the tumor declined steadily until the end of the study, and the histologically observed maturation of the tumor cells was reflected in this drop in DNA per unit weight of tumor tissues. A rise in the ribonucleic acid level in the tumorous tissues at this time cannot be as simply explained, although there is some evidence that changes in the level of RNA may be associated with the concomitant increase in the rate of protein synthesis.

Vitamins. Tumors of both sugar beet (Binet and Magrou, 1931; Berthelot and Amoureux, 1936c) and tomato (Nagy et al., 1937, 1938) contain much more ascorbic acid and glutathione than do healthy or non-tumorous tissues of tumorous plants, but usually less than that found in apical meristems of these plants. Henry, Riker, and Duggar (1942) reported high concentrations of thiamine in both young and mature crown-gall tumors of tomato. These data are too meager for evaluation.

Enzymes. Certain of the oxidases in tumor tissues have been studied, primarily those containing heavy metals. Harvey (1920), Klein and Zeise (1932, 1933), and Stapp and Pfeil (1939) found that catalase, peroxidase, and an "oxidase" (presumably tyrosinase) were high in beet tumors. Michaelis, Levi, and Hibbert (1943) and Levi, Michaelis, and Hibbert (1943) studied the respiratory inhibition of slices of healthy and tumorous beet tissues. Tyrosinase and peroxidase were significantly more active in tumors on a fresh weight basis, but ascorbic acid was less active in tumors than in the healthy tissues. The authors postulated that the increases in the concentration of ascorbic acid in tumor tissues were due to the decreased activity of the oxidase. Newcomb (1951) has reported that tissue cultures of sunflower and marigold crown-gall tissues have vigorous ascorbic acid oxidase systems. The amounts of cyanide-sensitive respiration of both tissues indicated that all of their oxygen uptake was mediated through heavy-metal-containing systems. Nagy et al. (1938) and Stapp and Pfeil (1939) found that catalase and peroxidase were more active in tomato crown-gall tissues than in normal stems or non-tumorous stems of tumor-bearing plants. They reported the presence of an active tyrosinase in the tumors, but were unable to demonstrate this enzyme in healthy stems. Link, Klein, and Barron (1952) found both tyrosinase and cytochrome oxidase activity in healthy tomato stems, and demonstrated that all of the oxygen uptake of the stem tissues was mediated by enzymes containing heavy-metal prosthetic groups. Link and Klein (1951) reported that cytochrome oxidase, tyrosinase, and an uncharacterized ("residual") metalloprotein enzyme are each responsible for about one-third of the oxygen uptake of normal stem tissues. In mature crown-gall tissues, however, the tyrosinase system accounted for three-fourths of the oxygen uptake, the remainder being directed through cytochrome and the "residual" systems. This finding is of general interest since DuBois and Potter (1942) reported that the cytochrome systems of cancer tissues are reduced in activity.

Respiration. The respiratory rates of crown-gall tissues may, under certain conditions, be considered a measure of the overall metabolic activity of the cells. Care must be taken to distinguish between the capacity of the cells to respire at high rates under conditions of in vitro experimentation (operable capacity) and the rates occurring in vivo (operating capacity), where other factors may be limiting (Warburg and Hiepler, 1952). Experiments on the respiration of crown-gall tumors deal mainly with manifestations of operable capacity. Neish and Hibbert (1943a) found that slices of beet tumors respired faster than slices of normal or of "healthy" tissues of the tumorous specimen. There was a well-developed Pasteur Effect in these tissues, but the Meyerhof Effect and lactic acid formation occurred only in normal tissues, alcoholic fermentation predominating in the tumor tissue. This was also noted by Berthelot and Amoureux (1936b), who suggested that aerobic fermentation occurs in beet tumors.

Calculated on a weight basis, the respiration of mature crown-gall tissues of tomato is considerably higher than that of comparable healthy tissues. Contiguous tissues showed intermediate values (Muller, 1935; Link and Goddard, 1951). If calculated on a nitrogen base, the results were more erratic. Eberts, Burris, and Riker (1951) reported that the $Q_{O_2}(N)$ of exhaustively washed slices of old tomato tumors was lower than that of healthy stem tissues. Klein (1952) was able to repeat this observation only when the tissues were quite old, e.g., at a time when protein synthesis had proceeded for some time and large quantities of nitrogen had accumulated in the cells of the tumor tissue. Link and Goddard (1951) found that tumor tissues from nitrogen-deficient tomato plants had the same high rates of oxygen uptake as tumor tissues from plants supplied with adequate nitrogen. These results were obtained even when the slices of tissue from the deficient plants contained less than half as much nitrogen as plants receiving adequate nitrogen. One must conclude that real differences in the respiration of normal and tumorous tissues are a function of some constant character of the cell. In view of the specific accumulation of nitrogen in mature beet and tomato tumors (Neish and Hibbert, 1940; Nagy et al., 1938), it would appear that total or protein nitrogen is not such a character. On the other hand, DNA may, in plants which do not show extensive polyploidy, be a suitable base, since it may be a measure of cell number. Klein (1952) found that slices of tomato crown-gall tissues possessed respiration rates which were consistently higher than those of comparable normal tissues.

Physiology and biochemistry of contiguous tissue. Mention has been made of those tissues which abut on tumors but show no structural indications of tumorization. These tissues, called "contiguous tissues" by Nagy et al. (1938) and "tumor ends" by Link and Goddard (1951), usually possess levels of biochemical activity intermediate between healthy tissues and tumorous tissues. They have, for example, intermediate rates of oxygen uptake (Link and Goddard, 1951), enzyme activity (Nagy et al., 1938), carbohydrate and nitrogen levels (Nagy et al., 1938; Neish and Hibbert, 1940), and ascorbic acid and glutathione levels (Berthelot and Amoureux, 1936a). Clearly, it is not permissible to use these parts of a tumor-bearing organ as the base for comparing the metabolism of normal and tumor tissues even though they show no detectable histological change. Failure to recognize this has resulted in confusion in the literature and has led to hypotheses of doubtful validity as to the biochemical nature of tumors. A less obvious but perhaps more important consequence of these findings is the possibility that contiguous tissues are in the process of secondary appositional tumor transformation. That histological and biochemical modifications are going on in these cells, attendant upon their alteration into tumor cells and their incorporation into the tumor mass, may be inferred by the gradual extension of the tumor into areas of the stem initially occupied by contiguous tissues. As the tumor progressively involves its upper and lower margins, contiguous tissues must be obtained higher up and lower down the stem (Link and Goddard, 1951). The structural changes which occur during this process have been detailed by Smith (1922) and Buvat (1945) and discussed earlier in this review.

Evaluation of biochemical data. Examination of the data on the comparative biochemistry of tumorous, healthy, and contiguous tissues of tomato stems and sugar beet roots reveals striking similarities for tumors on organs with quite different past histories, hereditary backgrounds, potentialities, and functions. Many characteristics of tumorous cells and tissues (cytological, histological, morphological, and biochemical, and physiological) show the same converging pattern. This is not to say that differences do not exist among tumors. These differences are apparent from studies on the utilization of nutrients by tissues in vitro (Riker and Hildebrandt, 1951), in the sensitivity of tumors to bacteria (Volcani, Riker, and Hildebrandt, 1953), and in studies of the sizes and growth rates of tumors induced on the same host by different strains of bacteria (Magrou, 1927, 1935; DeRopp, 1950a), or on different hosts by the same strain of bacteria (Kulescha, 1947a, b). In the main, these differences are variations in, but not alterations of, a generalized behavior pattern. Most crown-gall tumors follow fairly predictable courses of growth and development in vivo (Levine, 1921a) as well as in vitro. Levin and Levine (1920, 1922a) and Levine (1936, 1947) postulated that in vivo all crown-gall tumors pass through stages in a life cycle, viz., latent period, period of active growth, maturation, senescence, necrobiosis and death. In criticism of Levin and Levine's interpretation, A. C. Braun (pers. commun. to R. M. K., 1951) pointed out that mature, or even senescent, tumor cells can be made

to grow in vitro and will show the same capacity for growth as do cells taken from young tumor masses. Clearly, in vivo, a life history is easily seen. It is possible that the terminal stages in this life history are a result of inadequate vascularization, as is the case for certain animal neoplasms. Furthermore, maturation processes are due at least in part to the action of specific etiological agents and factors formed in the host or in the tumor mass. Although the behavior of cells forming a tumor appears unregulated and non-integrated relative to healthy cells, the tumor is sufficiently integrated to maintain characteristic growth patterns and biochemical capacities both in vivo and in vitro. It would, however, be somewhat premature to consider crown-gall tumors as new biological entities (Gäumann, 1948) proceeding according to their own rules and requiring or being subject to no regulation by their hosts. On the contrary, the recovery of tumor cells and their reversion to normal suggests that the growth pattern of the host cells, both genetic and non-genetic, is still present in the tumor cell; it apparently is overwhelmed by the tumorous state.

Role of Growth Substances

Some evidence is available which suggests that growth substances may be specifically required for the organization and differentiation of tumor cells. Link, Wilcox, and Link (1937) noted an initial dedifferentiation and subsequent excessive, localized differentiation in both auxin-induced neoplastic tissues and crown-gall tumor tissues. They postulated that the hyperauxiny of the tumor played an etiological role in both types of cellular response. Struckmeyer, Hildebrandt, and Riker (1949) and Levine (1950) observed that tissues of sunflower tumors cultured in vitro were composed of relatively simple cells, most of them being thin-walled, "hyperplastic" cells. Scalariform cells and giant cells were occasionally seen but comprised only a small percentage of the tumor mass (Gautheret, 1947). When fragments of tumor tissues were grown in media containing low concentrations of IAA, or other growth substances, the percentages of giant cells were significantly increased, and many more tracheal elements were formed (Gautheret, 1947; Struckmeyer, Hildebrandt, and Riker, 1949). These differentiated cells were lignified, like those of the tumors in vivo. Mention has previously been made of the hyperauxiny of tumor tissues in vivo and in vitro. Link and Eggers (unpub.) found that the auxin levels of tomato crown-gall tissues increased up to the time of differentiation. It is noteworthy that Jacobs (1952) has reported that auxin is specifically required for the differentiation of xylem elements following the mechanical rupture of vascular strands in internodes of *Coleus*. Skoog (1944) and Jacobs (1952) have suggested that the differentiation of xylem elements, both in normal and tumor tissues, is initiated by stimulation by growth substances.

If it should be definitely demonstrated that auxin is a component of the causal complexes of normal and abnormal cell differentiation it probably will be found that it plays its role as an internal environal factor originating in other cells of the plant under study. To what extent heredity, past history, etc., may play causal roles is not known.

Summary of Organization and Differentiation Period

The events occurring in the maturation stage of tumor growth may be summarized as follows: During the maturation stage, cellular differentiation and organization of the cells into tissues and a structurally complex tumor may occur. Once differentiation of cells is initiated, the tumor consists of a peripheral region where secondary transformation may proceed, regions of duplicating cells, and regions of cell differentiation. In some instances, sufficient differentiation and organization takes place to establish vascular connections with the host tissues, with resultant continued growth and development of the tumor. Some tumors are able to initiate root and shoot analogs, which may be tumorous in nature or may be the result of a recovery of cells within the tumor mass.

A number of biochemical differences between tumorous cells and tissues and their counterparts in normal organs have been observed. The differences to date have not been shown to be causally related to the tumor state. They are, however, evidences of changes in metabolism and potentiality of the affected cells.

SENESCENCE AND DEATH STAGE OF A TUMOR

Senescence Period and Necrobiosis and Necrosis Period

Whether the cellular events which characterize the senescence and death stage of the life history of a tumor comprise two types and periods of cellular change and behavior is not known. It may

eventually become desirable to subdivide the stages presented in this section.

Necrobiosis and necrosis are the dominant cellular and tissue events in the senescent and death stage of the life history of crown-gall tumors in vivo (see Figs. 1, 5). Excessive browning is one of the more striking evidences of these changes. It may occur on the surfaces of tumors which internally are still growing or are mature. In tomato tumors, localized necrotic areas may appear internally although the surface of the tumor is unaffected. The tumor may be poorly insulated, usually lacking an effective periderm or other protective surface (Fig. 8, B). As a result, it may be subject to excessive water loss in a dry atmosphere or to invasion by saprophytic or parasitic organisms in a damp atmosphere. In part, necrobiosis may result from nutritional deficiencies. Tumors usually are deficient in photosynthetic tissues and have poor vascular connections with the host, with resultant water and mineral deficiencies as well as shortages in carbohydrates and organic micronutrients which are usually supplied via the phloem. Furthermore, the very compactness of the tumor tends to prevent optimal gas exchange, and the cells may experience respiratory difficulties with attendant modifications in their metabolism. The accumulation of toxic end-products, alcohol, lactic acid, etc., probably occurs to an abnormal degree.

There is no literature on the cytology, histology, physiology, and ecology of senescent, necrobiotic, and necrotic tumor cells and on their etiologies. Presumably the findings on the cellular changes and behavior of senescent, necrobiotic, and necrotic cells of normal plant tissues are applicable here.

Effects of the Tumor on the Host

That the presence of crown-gall tumors has profound effects on the growth behavior and other characteristics of the host plant has been known since the pioneer work of E. F. Smith (1911). Beal (1944) has suggested the term "Telemorphic Response" to cover those morphological modifications of a plant which are induced or incited in tissues at a distance from the point of origin of the stimulus. Magrou (1928), Nemec (1930), Locke, Riker, and Duggar (1937, 1938), Link, Wilcox, and Link (1937) and others observed a variety of telemorphic responses in tumor-bearing tomato plants which are commonly associated with systematic hyperauxiny (Figs. 2, 3, 5). Link and Eggers (unpub.) have, in fact, demonstrated this hyperauxiny by biological assay of the auxin extracted from tumor-bearing tomato plants. Link et al. (1953) observed general systemic effects of growth substances on both cell enlargement and on cell division in both nitrogen-deficient and normal tumor-bearing tomato plants evidenced both in decreased height and diminished number of internodes. These effects were more severe on the deficient plant. The presence of a crown-gall tumor has equally striking physiological effects in the tissues of the host. Riker (1939) has, for example, shown that the circumference of young, tumor-bearing apple trees was below control values. Lopatin (1939) observed modifications in the water relations of tumor-bearing cherry trees.

Neish and Hibbert (1940) reported that the chemical composition of non-tumorous tissues of sugar beets bearing unilateral tumors differed from tissues of healthy beets. The levels of nitrogen and carbohydrate fractions were generally lower than in either healthy or in tumorous tissues. Klein (1952) noted nitrogen deficiencies in the apical internodes of tumor-bearing tomato plants. Tumors on plants grown under nitrogen-deficient conditions more severely restricted the growth in height, stem diameter, leaf formation, and percentage dry weight of the host tissues than those borne on plants grown under more favorable supplies of nitrogen (Link and Wilcox, 1936; Link et al., 1953) (Figs. 2, 3, 11, 12). In spite of the severe depressive effects of tumor development on the growth behavior of the host, the tumors formed on the woody, stunted, nitrogen-deficient plants were only slightly smaller in area, weight, or diameter than those borne on the vigorous plants receiving adequate supplies of nitrate-nitrogen. Relative to the size of the weight of the entire plants, tumors on the deficient plants were several-fold larger (Figs. 2, 3, 11, 12). These tumors on the deficient plants occasionally attained such an ascendency over the growing points in the mobilization of nutrients that the apex died although the tumor continued to grow (Fig. 12). Appler (1951) observed similar responses following inoculations into leaves. Thus, nitrogen-deficient plants, although deprived of an external source of nitrogen with attendant severe inhibition of their own growth, made available to the tumor sufficient nitrogenous material for almost optimal tumor growth. The ability of tumors borne on these deficient plants to grow at rates comparable to those on plants under more adequate nutrient

levels indicates that, to some extent, the growth rates of tumors are independent of those of healthy host cells and tissues, and that tumor tissues possess unusual growth potentials. This hypothesis is supported by the results of Klein and Klein (1952), who found that a fifty per cent suppression of the growth and development of tomato plants by maleic hydrazide was not reflected either in the growth rates or the final weights of the tumors borne on those plants. In general, the more severely the host is affected by external factors and events, the more severely the tumor will affect the metabolism of that host.

There is good evidence that the presence of a tumor will influence the development of another tumor borne on the same plant. Riker and Berge (1935) cited several instances where inoculations into stems at sites close to a tumor have either failed to induce new tumor formation or have resulted in small tumors. These authors have rejected the hypothesis that these inhibitions were due to immune bodies produced by the host in response to the initial inoculation. This question has been discussed in an earlier section of the review. Link et al. (1953) inoculated tomato plants simultaneously in basal, middle, and apical internodes of the same plant or into basal and apical internodes only. Apical tumors showed the greatest area or weight increase, with the middle and basal tumors following in that order. These differences were ascribed to alterations in the morphogenetic and physiological "age" of the internodes inoculated, as well as to nutritional and position effects of one tumor relative to the others.

The ability of crown-gall tumors to mobilize nutrients from their hosts suggests that the tumor has become dominant over some or all other centers of meristematic activity (Link et al., 1953) (Figs. 2, 3, 11, 12). Link and Goddard (1951) found that the percentage total nitrogen of tumors borne on nitrogen-deficient plants or on plants with adequate nitrogen were higher in comparable control tissues, the relative ratio of accumulation being greatest in the deficient plants. The accumulation of phosphorus and of other inorganic substances tends to confirm this observation (Manigault, 1953).

ROLES AND MODES OF ACTION OF ETIOLOGICAL FACTORS

This review of the etiology of crown-gall has followed normal cells through the numerous structural and physiological changes involved in their transformation into tumor cells and through various other stages in the genesis of a crown-gall tumor. Wherever possible, the sources and the nature of known and presumed etiological factors which are involved in the cellular changes characteristic or dominant in the stages in the life history of a tumor have been discussed. Consideration of the modes of action of these etiological factors and agents was deferred because speculation of this type at the point in the text where the agent was first discussed would have been based on incomplete information. At the present point, the possible modes of action of the three etiological agents known to bring about primary transformation will be discussed. Although hypotheses in regard to the relation of these agents, and their affected cells, to secondary transformation will be entertained, no effort is made to include information on the other etiological factors known to be involved in transformation.

Wound Substances

The necessity for wound substances in the responses leading to wound-healing in plants has been known for many years (Bloch, 1941). They also seem to be specifically required for the activation or conditioning of those cells which are to be acted upon by the other tumor-inducing agents. Link and Eggers (unpub.) showed that wounded, and wounded and inoculated, tomato hypocotyls yield ether extracts which auxinically are more active than extracts of the controls. This enhanced auxinic activity may be due to "wound auxins." The extracts of wounded inoculated hypocotyls were more active than those of the merely wounded. Recent work has, in addition, suggested that wound substances are also required for the production of TIP by virulent crown-gall bacteria (Klein and Knupp, unpub.). This finding suggests that wound substances may contain the proper precursors for specific bacterial synthesis of TIP, and possibly also provide satisfactory physical conditions (buffer action, enzyme protection, etc.) for this synthesis. The fact that wound substances are also required for the recrudescence of the meristematic activity which leads to callus formation and wound-healing indicates that the activation processes in tumor-cell formation and in wound-healing may be identical. Conditioned cells, unless immediately exposed to TIP, will become callus cells. It is possible that wound substances merely supply high concentrations of compounds needed by the cell for protein and

enzyme synthesis as well as for respiratory activation, as a result of which the cells are shifted into meristematic activity. Other actions might include alterations in the permeability of the cell walls permitting the entrance of precursors necessary for growth. Braun (1952b) postulated that wound substances incite the formation of one or more normal cell components in abnormally high concentrations and that these are responsible for the predisposition of the cells to TIP. When wound healing begins, these cell components are presumably restored to normal levels by dilution among the new cells, and wound-healing stops. When dilution of these components per cell occurs by the division of callus cells, they are no longer responsive to the action of TIP. Although available experimental data can be well integrated within the framework of this hypothesis, additional work is required before it can be considered adequate.

Tumor-Inducing Principle

The demonstration that TIP, a heat-labile product of virulent crown-gall bacteria, is an etiological agent in the alteration of a conditioned cell into an incipient tumor cell, permits an evaluation of those hypotheses which attempt to account for the mode of its action. These hypotheses may be divided into two major categories: (1) TIP enters a conditioned cell and is, per se, the permanent agent of change; or (2) TIP is not the permanent agent of change but alters or evokes modifications in the ultra-structure of the cells (including genes, cytoplasmic entities, enzyme systems, etc.), the altered cell components being the permanent directive mechanism of the tumor cell.

TIP as the agent of change. Included in this first category are those hypotheses which assume that the inducing agent is a virus. D'Herelle and Peyre (1927) implicated a "protobacterial" entity obtained by lysis of the bacteria by a specific bacteriophage as being this agent. Israilsky (1927), Kauffmann (1928), Muncie and Patel (1929), Thung (1929), and Brown and Quirk (1929) all found that 'phage-lysed populations of bacteria or filtrates of the bacteria-phage mixtures were either completely avirulent or had reduced virulence. Bechhold and Smith (1927) reported that a special filtrate of crown-gall bacteria, which they termed "tumefaciens-plastin," was the tumor-inducing factor. Kauffmann (1928) demonstrated that this plastin did not exist and that the filtration techniques of Bechhold and Smith permitted contamination of the filtrates by bacteria. Other dissociated forms of crown-gall bacteria have been considered the "cause" of crown gall (Riker and Berge, 1935). In general, the experimental evidence invoked to support these hypotheses has not been at all convincing (Stapp and Bortels, 1931).

DeRopp (1951c) suggested that TIP might be a virus vectored by virulent crown-gall bacteria. The report that TIP may be a macromolecular entity, possibly a polymerized DNA, formed in quantity only under special conditions and inactivated by moderately elevated temperatures, is not incompatible with the hypothesis that a virus is the agent which brings about induction of a primary tumor-cell. Several considerations, however, militate against this hypothesis (Gautheret, 1952b). The report that inoculations of cultures of 'phage-lysed cells, from which a virus would presumably have been freed, did not result in tumor-cell formation (Muncie and Patel, 1929), and the suppression of tumor formation by application of antibiotics to inoculated tissues (DeRopp, 1950b), both throw doubt on the lysogenic-virus hypothesis, as does the absence of virus inclusion bodies from tumor cells (Black, 1954). It is known that viable, uninjured bacteria are necessary for the multiplication of this hypothetical virus. Klein and Klein (1953) tried without success to establish the presence of a lysogenic virus in crown-gall bacteria, and Camus (pers. commun. to R. M. K., 1952) has confirmed these negative findings. White and Braun (1942) were unable to transmit any crown-gall stimulus with homogenates of tumor cells. Extracts of bacteria-free tissues were unable to alter avirulent bacteria into virulent forms (Klein and Klein, 1953). Camus et al. (1951) attempted to isolate a virus from tumor tissues by electrophoresis and ultracentrifugation and have reported that they observed an unusual nucleoprotein component in their preparations. No report on the tests of the biological activity of this component and no details of their methods are available to permit an evaluation of these potentially important findings. Braun (1954) appears to have found serologically distinct proteins in tumor tissues.

Another line of evidence bearing on the validity of the virus hypothesis is to be found in studies dealing with the experimental acquisition of virulence by avirulent bacteria (Klein and Klein, 1953). Those authors postulated that these "trans-

formation reactions" are unlikely to involve the infection of the altered bacterium by a virus and indicated that a hereditary unit of the bacterium is acquired by the altered bacterium. The possibility that an hereditary unit of a bacterium is biologically active in cells of a higher plant is somewhat remote. Further, the transforming agent was not active in plant tissues. Finally, in distinct contrast to typical prophages or viruses, the transforming agent for the bacteria was inactivated by desoxyribonuclease.

It has also been suggested that TIP enters the nucleus of the affected cell and acts as a gene. By a rigorous application of the hypothesis that tumor-cell recovery is effected by dilution of replicating cytoplasmic entities, this suggestion may be eliminated. If the word "gene" is restricted to a hereditary determinant borne on a chromosome (Lederberg, 1952), it is clear, since recovered shoots may flower and set normal seed, that recovered shoots are genetically identical with the tissues from which they were initially derived. The unlikelihood that TIP can be eliminated from a gene locus by dilution favors the position that TIP does not function as a gene (cf. Fardon, 1953).

One may postulate that TIP functions as a hereditary unit in the cytoplasm of the altered cell, becoming an endosymbiont in the sense given it in the terms in Lederberg's (1952) terminology. No direct evidence is available for evaluating this hypothesis. Assuming that TIP is, in fact, a specific polymer of DNA, it might be possible to find it in the cytoplasm of tumorous cells. Klein, Rasch, and Swift (1953) were unable to observe any cytoplasmic DNA, although a special effort was made to do so. This failure does not entirely eliminate the possiblity that TIP functions as an endosymbiont, since the cytochemical techniques now available may not be adequate to detect it in the cytoplasm. If TIP functions as an endosymbiont, its concentration should remain high throughout the life of the tumor cell. The finding of a decrease in the level of DNA, which may represent the titer of TIP, by the end of the Induction Phase of the Transformation Period, however, does not fit this hypothesis (Klein, 1952, 1953; Klein, Rasch, and Swift, 1953), although only a very few molecules of TIP may be necessary for induction; the remainder would then disappear. Finally, the fact that plant tissues have been heated to 47°C. for prolonged periods of time, (a temperature some 20°C. higher than the inactivation temperature of TIP), without altering the capacity of the tumor cells to survive as such, suggests that the agent responsible for tumor-cell characteristics is not TIP. It is most reasonable to assume that TIP is an initiating factor and not itself the factor which maintains cells in the tumor state.

TIP as the evoking agent of the entity of change. Among others, DeRopp (1951c) has suggested that TIP may induce a somatic mutation of one or more of the genes. This hypothesis is confronted with several difficulties. Because of the precise and reproducible nature of the tumorous alteration, it must be inferred that if genes are involved they are readily mutable and mutate in a predictable manner almost 100 per cent of the time. Although directed mutations are known, it is improbable that plants of different taxonomic groups all possess the same mutable alleles. In addition, these presumed mutated genes must control master reactions, since a wide range of structural characters and physiological activities are modified in tumor cells. From the evolutionary point of view, it would not be expected that those genes which control such reactions would be readily mutable. Etiologically, too, the gene mutation hypothesis is unsatisfactory, since activation by wound substances and the promoting action of auxins do not appear to be etiological factors in gene mutation. Genes are not subject to the effects of dilution unless it is assumed that rapid cell division is of significance in directed back mutations. This is most improbable.

Braun (1952b) has indicated that the agents which maintain the tumor state are duplicating cytoplasmic entities capable of overwhelming, but not of destroying, the regulatory mechanisms of the cell. That these entities have hereditary continuity is readily seen in the ability of tumor tissues to maintain the tumor state indefinitely in vitro. We may use the general term *plasmid* (Lederberg, 1952) for such an entity, and the term *"crown-gall plasmid"* for the one possibly involved in crown gall. No effort will be made to discuss the evidence demonstrating the existence and activity of plasmids. For our purposes it will be assumed that they exist, that they may control and regulate cell behavior, and that they may be modified (mutated) or evoked under appropriate conditions.

Three mechanisms can be visualized whereby TIP may affect plasmids: (a) by fixing permanently the numbers of plasmids present at the time of

Induction; (b) by evoking the formation of new plasmids; or (c) by altering (mutating) existing normal plasmids. In each of these mechanisms, the TIP could act either directly by conjugation with preexisting entities, or indirectly, through its action on the mechanisms which regulate plasmids. As indicated above, the conjugation hypothesis is the least satisfactory. On the assumption that a DNA, viz., TIP, is the inducing agent, its titer, if it conjugated, should remain high after the end of the Induction Phase of the Transformation Period.

The first of these possibilities (plasmid fixation) has been discussed in detail by Braun (1952b). On the assumption that the plasmid content of a normal resting cell is precisely regulated and that there may be changes in their numbers or in their functions when the cell is activated by wound substances, conditioning by wound substances might favor the replication of those plasmids which direct the division of wound-repair cells. These assumed modifications in plasmid number would, in turn, be completely under the control of the host, so that their numbers would be restored to normal at the completion of the healing process. Under conditions of fixation by TIP those capacities which were controlled by the numbers of modified plasmids should continue. Thus, the time required for conditioning would represent that period necessary for cells to acquire the optimal numbers of plasmids to result, after fixation, in the formation of an incipient tumor cell. This hypothesis, although attractive, is not without disturbing features. Basically, it suggests that crown-gall tumor cells are permanently activated wound-healing cells. Were this true, the biochemical and cytochemical properties of tumor cells should be identical with those observed during the first few days after wounding of normal tissues. This is not the case (Muller, 1935; Link and Goddard, 1951; Klein, 1952; Klein, Rasch, and Swift, 1953). In addition, the existence of other unusual metabolic and growth patterns in tumor tissues relative to wound-healing tissues has been noted (cf. Friedemann and Magnus, 1915; Magnus, 1918; Bloch, 1941). As far as can be determined, tumor cells are not permanently activated wound-stimulated cells.

It is, at present, impossible to differentiate between a specific formation of crown-gall plasmids and the alteration (mutation) of preexisting plasmids. Woods and DuBuy (1951) and Rose (1952) have indicated that certain preexisting plasmids may be modified from normal- into tumor-determinants. Growth of the Rous sarcoma I, for example, has been shown to be determined by a nucleoprotein-lipid particle in the cytoplasm. Wright (1945) and Woods and DuBuy (1951) believed that cytoplasmic components are only partly autonomous, in that their persistence, multiplication, and mutation are under gene control. These suggestions may offer a fruitful lead towards explaining the failure of all monocots and even some dicots to show tumor formation. Another lead is to be found in the specificity of a particular TIP produced by a strain of the bacteria.

As an alternative to the hypothesis that TIP merely fixes the numbers of plasmids in an activated cell, it is here postulated that activation or conditioning of normal cells consists in the acquisition of a "plastic" state by the cytoplasmic determinants of the conditioned cell. In this state, well known for bacteria, certain of the plasmids may be positively disposed to alteration into crown-gall plasmids by TIP. These altered plasmids then would be capable of directing the formation and the activities of enzyme systems (Spiegelman, 1945, 1946), morphogenetic determinants (Woods and DuBuy, 1951; Wright, 1945), and the factors which determine the autonomy of the resulting incipient tumor cell (or tumor cell, vide Braun, 1952b). Braun (1953c) has made a similar suggestion with respect to alteration of cytoplasmic entities. Since these plasmids are different from the normal plasmids of the cell, they may replicate at rates different from those still unaltered and conceivably be diluted out of rapidly dividing cells. One indication that crown-gall plasmids are qualitatively different from those characteristic of normal plasmids is to be seen in the altered metabolic pathways of tumor cells relative to cells that show only quantitative alterations in metabolic patterns.

It is further suggested that crown-gall plasmids from tumor cells may migrate across cell walls into normal cells. Replication of these entities in the invaded cell might alter them progressively into secondary tumor cells and result in the phenomenon of appositional growth. Newcomer (1951) has presented data indicating that an intercellular movement of cytoplasmic particles via the bridges provided by plasmadesmatal strands may occur. The occurrence of secondary tumors

without tumor-strand connections might have a similar basis, although the failure of the intervening cells to act as hosts for the crown-gall plasmids is difficult to explain.

If TIP does alter cytoplasmic entities or evoke new ones, a search must be made to identify them. Assuming that these entities may be special mitochondria (and it is equally possible that any observed mitochondrial alterations might be the result of the activities of other plasmids), the problem of mitochondria in tumor tissues deserves serious attention. Newcomer (1951) demonstrated that the numbers of mitochondria in plant cells are greatest in actively dividing cells and apparently are associated with high levels of metabolic activity. Spiegelman (1945, 1948) has reported that their numbers and activities are influenced by the conditions acting on the cells, i.e., by the hereditary constitution, past history, and the action of any etiological factors and agents on the cell at a given time. Mitochondria are capable of competing with one another for the materials needed for their replication and activity. Under special conditions, this competition may result in the selective replication and eventual dominance of one type over another. Many workers have shown that mitochondria possess the capacity for replication at controlled rates. Brachet (1947) has detailed the data which show the relationships among mitochondria and of heredity, enzymatic activity, and the regulation of biochemical activities. Mitochondria are essential for enzyme synthesis (Spiegelman, 1946). There is a body of data which shows that the mitochondria of crown-gall tumor cells are quantitatively and qualitatively different from those of normal cells. Quantitative differences have been observed by Buvat (1945), who reported increased numbers in tumor cells of tomato. Qualitative differences have been observed in cytochrome oxidase activity (Link and Klein, 1951) and in phosphorylative capacity (Klein, 1952). Both of these activities are localized within mitochondria (McClendon, 1953; Bonner and Millerd, 1953). The loss of chloroplastids during tumor genesis and their reappearance following recovery suggest that the mitochondria play a role in the induction and the maintenance of the tumor state. Potter et al. (1950) have stated that carcinogenesis in animals may involve alterations in the rates of replication of mitochondria and have demonstrated these differences by direct counts. To date, these studies have not been extended to plant neoplasms. It is of interest that Stasney et al. (1952) have been able to transmit animal tumors by the injection of the cell organelles of tumor cells initially incited by a chemical carcinogen. Studies to determine the relation of these findings to plants offer an exciting future in crown-gall research.

Growth Substances

It has been indicated that growth substances play at least four distinct etiological roles in the initiation and development of a crown-gall tumor. Auxins are required for the promotion of incipient into primary tumor cells. They also play a role in the duplication of tumor cells, and possibly in their differentiation. Finally they are active in the causal complexes of the general host effects which accompany the genesis and development of the tumor. [If Braun's proposition is accepted, then only the wound auxins play a role in the period of primary transformation.]

If auxins are required during primary tumor-cell transformation, this does not imply that they are the primary tumor-inducing agents. There are no structural (Kulescha, 1947c), morphological (DeRopp, 1947c; Kulescha, 1951), biochemical (Link and Klein, 1951; Klein, Rasch, and Swift, 1953), or etiological (Gautheret, 1946, 1953) grounds for the proposition that the cells of a crown-gall tumor are such merely because of the stimulus provided by an endogenous supply of auxin. Even if consideration of auxinic autotrophy of tumor cells is laid aside, the numerous biochemical and morphogenetic criteria which distinguish the cells of crown-gall tumors from those of other neoplastic growths preclude the possibility that they are essentially identical.

The mode of action of growth substances acting as conditioning and promoting agents is not understood. In view of the lack of specificity of the compounds used to promote incipient tumor cells, it is most reasonable to assume that promotion involves conditioning and stimulation of those cell activities which result in the preparation for division. It may be that the action of auxins in these activities of prospective tumor cells does not differ from its role in the division of normal cells. Audus (1953) has assembled most of the pertinent findings relative to the affects and effects of growth substances in the growth and development of plants. Gordon (1953) has reviewed the literature on the physiology of hormone action and (1954) on the occurrence,

formation, and inactivation of auxins, with discussion of the mechanism of the action of auxins and their physiological roles. He is of the opinion that very little is positively known about the physiological mode of action of auxins. It may be postulated that auxin merely provides the conditions necessary for cell enlargement and eventual division to proceed rapidly. Heyn (1940) reviewed the literature on cell enlargement and associated processes in relation to auxin action. He concluded that auxin was specifically required by the cell to permit plastic extensibility of cell walls during cell enlargement and subsequent division. Studies on the biological relationships of growth substances to water uptake, respiration, protein synthesis, and other vital processes in plant cells have been underway for many years (Skoog, 1947), and evidence is accumulating that the enhanced metabolism of the *promoted* cells is similar to that of normal cells stimulated by auxins.

Obviously, the etiology of crown-gall is far from complete. The crown-gall problem has not yet "been solved." Biological and biochemical techniques are not yet refined enough to answer many of the etiological questions presented at the cellular level of bio-organization by crown-gall. When they have been solved, biology will have advanced far along the trail of elucidation and understanding of fundamental biological problems of cyto-histo-organo- and morpho-genesis.

The procedure of subdividing the overall event of a tumor's life history into a series of stages and these into a series of temporal "time slabs" or part-events of cellular occurrences and behavior has proven fruitful in advancing progress in the study of crown-gall. It has also made possible the effective use of the concept of a causal complex and has permitted its application to the various part-events. It has revealed the role of wounding, of the tumor-inducing principle, and of auxin as necessary, but not sufficient causal agents in the initiation of a crown-gall tumor and of its development, and in the initiation and development of affects and effects distant from the site of the tumor.

ACKNOWLEDGMENTS

The preparation of this review was aided in part by a grant to G. K. K. Link from the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago, and by a fellowship to R. M. Klein, while in the Department of Botany, University of Chicago, from the American Cancer Society through the Committee on Growth, National Research Council. Additional support for typing and publication was given by the Department of Botany, University of Chicago, and by the New York Botanical Garden.

Thanks are due the *Botanical Gazette* for permission to republish Fig. 1 and to the *American Journal of Botany* for permission to republish Figs. 2, 3, 9, and 10. Special thanks are due Drs. Marjorie Anchel, Deana T. Klein, and W. J. Robbins for their helpful criticism.

LIST OF LITERATURE

APPLER, H. 1951. Über die Tumorbildung durch *Pseudomonas tumefaciens* und durch Heteroauxin an *Helianthus annuus*. *Biol. Zbl.*, 70: 452–469.

ARNAUDI, C. 1925. Sull immunita acquisita nei vegetali. *Atti Soc. ital. Sci. nat.*, 64: 230–238.

——. 1928. Nuove esperienze sulla vacinozione della piante. *Riv. Pat. veg. Padova*, 18: 161–168.

ARK, P. A. 1937. Effect of certain enzymes and amino acids on crown-gall tissues. *Science*, 85: 364.

——. 1941. Chemical eradication of crown-gall on almond trees. *Phytopathology*, 31: 956–957.

——. 1947. Effect of crystalline streptomycin on phytopathogenic bacteria and fungi. *Phytopathology*, 37: 842.

AUDUS, L. J. 1953. *Plant Growth Substances*. 465 pp. Leonard Hill, London.

BANFIELD, W. H. 1934. Life history of the crown-gall organism in relation to its pathogenesis on the red rasberry. *J. agric. Res.*, 48: 761–787.

——. 1935. Studies in cellular pathology. I. Effects of cane-gall bacteria upon gall tissue cells of the black rasberry. *Bot. Gaz.*, 97: 193–239.

BEAL, J. M. 1944. Some telemorphic effects induced in sweet pea by application of 4-chlorophenoxyacetic acid. *Bot. Gaz.*, 105: 471–474.

BECHHOLD, H., and L. SMITH. 1927. Tumefaciensplastin. *Z. Krebsforsch.*, 25: 97–104.

BERTHELOT, A., and G. AMOUREUX. 1936a. Sur les tumeurs obtenues par inoculation de *Bacterium tumefaciens* à des plantules et des jeunes plantes cultivées aseptiquement. *C.R. Acad. Sci., Paris*, 203: 629–631.

——, and ——. 1936b. Recherches sur le composition chimique des tumeurs de la Betterave determinées par *Bacillus tumefaciens*. *C.R. Soc. Biol., Paris*, 123: 942–944.

——, and ——. 1936c. Sur la teneur en glutathion et en acide ascorbique des tumeurs de la Betterave determinées par *Bacillus tumefaciens*. *C.R. Soc. Biol., Paris*, 123: 944–946.

——, and ——. 1938. Sur la formation d'acide

indol-3-acètique dans l'action de *Bacterium tumefaciens* sur le tryptophane. *C.R. Acad. Sci., Paris*, 206: 537–540.

BERRIDGE, EMILY H. 1930. Studies in bacteriosis. XVII. Acidic relations between the crown-gall organism and its host. *Ann. appl. Biol.*, 17: 280–283.

BINET, L., and J. MAGROU. 1931. Glutathion, croissance et cancer des plantes. *C.R. Acad. Sci., Paris*, 192: 1415–1416.

BITANCOURT, A. A. 1949. Mechanisms genetico da tumori sacao nos vegetais. Genetics Conference, São Paulo, Brazil.

——, K. SCHWARTZ, and R. DIERBERGER. 1954. La nature des auxines des tumeurs vegetale. *C.R. Sci. Biol., Paris*, 148: 822–825.

BLANCHARD, F. A. 1951. Aureomycin chemotherapy of crown-gall in tomatoes. *Phytopathology*, 41: 954.

BLOCH, R. 1941. Wound healing in higher plants. *Bot. Rev.*, 7: 110–146.

——. 1952. Wound healing in higher plants. II. *Bot. Rev.*, 18: 655–679.

BLUMENTHAL, F., and H. HIRSCHFELD. 1917. Untersuchungen über böseartige Geschwulste bei Pflanzen und ihre Erreger. *Z. Krebsforsch.*, 16: 51–58.

——, and ——. 1922. Beiträge zur Kenntnis einiger durch *Bacterium tumefaciens* hervorgerufenen Pflanzengeschwulste. *Z. Krebsforsch.*, 18: 110–125.

BOIVIN, A., M. MARKE, L. MESROBIANU, and P. JUSTER. 1935. Sur l'existence dans le *Bacillus tumefaciens* d'une endotoxine capable de provoquer la formation de tumeurs chez les vegetaux. *C.R. Acad. Sci., Paris*, 201: 984–986.

BONNER, J., and J. ENGLISH. 1938. A chemical and physiological study of traumatin, a plant wound hormone. *Plant Physiol.*, 13: 331–348.

——, and ADELE MILLERD. 1953. Oxidative phosphorylation by plant mitochondria. *Arch. Biochem.*, 42: 135–148.

BORTHWICK, H. O., K. C. HAMMER, and M. W. PARKER. 1937. Histological and microchemical studies of the reactions of tomato plants to indoleacetic acid. *Bot. Gaz.*, 98: 491–519.

BOUREQUET, R. 1952. Action de la mercaptoethylamine et de la mercaptothiozoline sur quelques tissus vegetaux cultivés in vitro. *C.R. Acad. Sci., Paris*, 235: 811–812.

BRAKKE, M. K., and L. G. NICKELL. 1952. Lack of effect of plant growth regulators on the action of alpha amylase secreted by virus tumor tissue. *Bot. Gaz.*, 113: 482–484.

BRAUN, A. C. 1941. Development of secondary tumors and tumor strands in the crown-gall of sunflower. *Phytopathology*, 31: 135.

——. 1943. Studies on tumor inception in the crown-gall disease. *Amer. J. Bot.*, 30: 674–677.

——. 1947a. Thermal studies on the factors responsible for tumor initiation in crown-gall. *Amer. J. Bot.*, 34: 234–240.

——. 1947b. Recent advances in the physiology of tumor formation in the crown-gall disease of plants. *Growth*, 9: 325–337.

——. 1948. Studies on the origin and development of plant teratomas incited by the crown-gall bacterium. *Amer. J. Bot.*, 35: 511–519.

——. 1950. Thermal inactivation studies on the tumor-inducing principle in crown-gall. *Phytopathology*, 40: 3.

——. 1951a. Cellular autonomy in crown gall. *Phytopathology*, 41: 963–966.

——. 1951b. Recovery of tumor cells from effects of the tumor-inducing principle in crown-gall. *Science*, 113: 651–653.

——. 1951c. Recovery of crown-gall tumor cells. *Cancer Res.*, 11: 839–844.

——. 1952a. Conditioning of the host cell as a factor in the transformation process in crown-gall. *Growth*, 16: 65–74.

——. 1952b. The crown-gall disease. *Ann. N. Y. Acad. Sci.*, 54: 1153–1161.

——. 1953a. Organization of crown-gall tumor cells in the presence of a formative stimulus. *Phytopathology*, 43: 204–205.

——. 1953b. Bacterial and host factors concerned in determining tumor morphology in crown-gall. *Bot. Gaz.*, 114: 363–371.

——. 1954a. Studies on the origin of the crown-gall tumor cell. Symp. on Abnormal and Pathological Plant Growth. *Brookhaven Symp. Biol.*, 6: 115–127.

——. 1954b. The physiology of plant tumors. *Annu. Rev. Pl. Physiol.*, 5: 133–162.

——, and T. LASKARIS. 1942. Tumor formation by attenuated crown-gall bacteria in the presence of growth-promoting substances. *Proc. nat. Acad. Sci., Wash.*, 28: 468–477.

——, and R. J. MANDLE. 1948. Studies on the inactivation of the tumor-inducing principle in crown-gall. *Growth*, 12: 255–269.

——, and G. MOREL. 1950. A comparison of normal, habituated, and crown-gall tumor tissue implants in the European Grape. *Amer. J. Bot.*, 37: 499–501.

BRAUN, A. C., and U. NAF. 1954. A non-auxinic growth-promoting factor present in crown-gall tumor tissue. *Proc. Soc. exp. Biol., N. Y.*, 86: 212–214.

——, and P. R. WHITE. 1943. Bacteriological sterility of tissues derived from secondary crown-gall tumors. *Phytopathology*, 33: 85–100.

BRAUN, W. 1952. Studies on population changes in

bacteria and their relation to some general biological problems. *Amer. Nat.*, 86: 355–371.

BROWN, J. G. 1948. Cytological effects of penicillin and streptomycin on crown-gall. *Phytopathology*, 38: 3.

——, and ALICE M. BOYLE. 1944a. Penicillin treatment of crown-gall. *Science*, 100: 528.

——, and ——. 1944b. Effect of penicillin on a plant pathogen. *Phytopathology*, 34: 760–761.

——, and ——. 1945a. Application of penicillin to crown-gall. *Phytopathology*, 35: 521–524.

——, and ——. 1945b. Crown-gall cured with crude penicillin. *Desert Pl. Life*, 17: 89–95.

BROWN, NELLIE A. 1923. Experiments with paris daisy and rose to produce resistance to crown gall. *Phytopathology*, 13: 87–99.

——. 1929. The tendency of the crown-gall organism to produce roots in conjunction with tumors. *J. agric. Res.*, 39: 747–766.

——. 1939. Colchicine in the prevention, inhibition, and death of plant tumors. *Phytopathology*, 29: 221–231.

——. 1942. The effect of certain chemicals, some of which produce chromosome doubling, on plant tumors. *Phytopathology*, 32: 25–46.

——, and F. E. GARDNER. 1937. Galls produced by plant hormones including a hormone extracted from *Bacterium tumefaciens*. *Phytopathology*, 26: 708–713.

——, and ——. 1937. Indole-acetic acid galls of a secondary type. *Phytopathology*, 27: 1110–1113.

——, and AGNES J. QUIRK. 1929. Influence of bacteriophage on *Bacterium tumefaciens*, and some potential studies of filtrates. *J. agric. Res.*, 39: 503–530.

BUVAT, R. 1943. Phénomènes de dédifferentiation dans les tumeurs corticales produites chez la tomate. *C.R. Acad. Sci., Paris*, 216: 127–129.

——. 1945. Recherches sur la dédifferentiation des cellules vegetales. *Ann. Sci. nat., bot.*, (11) 6: 1–106.

BURKHOLDER, P. R., and L. G. NICKELL. 1949. Cultivation of virus tumors of *Rumex* on nutrient agar. *Bot. Gaz.*, 110: 426–437.

CAMUS, G., and R. J. GAUTHERET. 1948a. Sur la transmission par greffage des propriétés tumorales des tissus de crown gall. *C.R. Soc. Biol., Paris*, 142: 15–16.

——, and ——. 1948b. Nouvelles recherches sur le greffage de tissus normaux sur des fragments de racines de Scorsonere cultivés in vitro. *C.R. Soc. Biol., Paris*, 142: 789–791.

——, and ——. 1948c. Sur le repiquage des proliférations enduites sur des fragments de racines de Scorsonere par des tissus de crown gall et des tissus ayant subi le phénomène d'accoutumance aux hetero-auxines. *C.R. Soc. Biol., Paris*, 142: 771–772.

——, S. G. WILDMAN, and J. BONNER. 1951. Comparative study of the soluble proteins of crown gall and normal tissues of sunflower cultivated in vitro. *Bull. Amer. Inst. biol. Sci.*, 1: 34.

CARBONE, D., and C. ARNAUDI. 1930. L'immunita nella piante. *Monogr. Ist. sieroter., Milano.*

CHARGAFF, E., and M. LEVINE. 1936. Chemical composition of *Bacterium tumefaciens*. *Proc. Soc. exp. Biol., N. Y.*, 34: 675–677.

COLEMAN, L. C. 1950a. Tumor induction in *Vicia faba* and other hosts by *Agrobacterium rubi*. *Canad. J. Res.*, C, 28: 277–282.

——. 1950b. Nuclear conditions in normal stem tissue of *Vicia faba*. *Canad. J. Res.*, C, 28: 382–391.

COLEMAN, MADELINE F., and J. J. REID. 1949. The conversion of strains of *Alcaligenes radiobacter* and *Phytomonas tumefaciens* in the "S" phase to the "M" phase of the heterologous species. *Phytopathology*, 39: 182–190.

COLASITO, D. J., H. KOFFLER, P. A. TETRAULT, and H. C. REITZ. 1951. Antibiotic effects of circulin against certain gram-negative plant pathogens. *Proc. Soc. exp. Biol., N. Y.* 77: 107–108.

COOK, M. T. 1923. Early stages of crown gall. *Phytopathology*, 13: 476–482.

DAME, F. 1937. *Pseudomonas tumefaciens*, der Erreger des Wurzelkropfes, in seiner Beziehung zur Wirtspflanze. *Zbl. Bakt.*, (II) 98: 385–429.

DARPOUX, H. 1950. Les antagonismes microbiens et les substances anti-biotiques en agriculture. 49 pp. Bull. Stat. Centrale Path. Veg. Versailles.

DECAPITE, L. 1952. Action du paraaminophenylsulfamide et de l'acide paraaminobenzoique sur le parenchyme vasculaire de Topinambour et sur les tissus de crown-gall de Scorsonere cultivés in vitro. *C. R. Acad. Sci., Paris*, 234: 2478–2480.

DEMAREE, J. B., and N. R. SMITH. 1952. Blueberry galls caused by a strain of *Agrobacterium tumefaciens*. *Phytopathology*, 42: 88–90.

DEMETRIADES, S. 1953a. Action du bleu d'aniline et du rouge de chlorophenol sur la formation et la croissance des tissus de crown gall. *C.R. Soc. Biol., Paris*, 147: 280–282.

——. 1953b. Sur l'action cancerigène de l'endotoxine de l'*Agrobacterium tumefaciens*. *C.R. Soc. Biol., Paris*, 147: 282–283.

——. 1953c. Sur un cas de differentiation des tissus de crown-gall de Scorsonere cultivés in vitro. *C.R. Soc. Biol., Paris*, 147: 1713–1715.

——, and J. P. NITSCH. 1953. Jus de tomate et croissance des tissus et organes vegetaux. Action sur trois catégories de tissus de vigne-vierge et du Scorsonere. Comparaison avec le lait de coco. *C.R. Soc. Biol., Paris*, 147: 1711–1713.

DERMEN, H., and NELLIE A. BROWN. 1940a. A cytological study of the effect of colchicine on plant tumors. *Amer. J. Cancer*, 38: 169–190.

——, and ——. 1940b. Cytological basis of killing plant tumors with colchicine. *J. Hered.*, 30: 197–199.

DE ROPP, R. S. 1946. Penicillin as a plant hormone. *Nature, Lond.*, 158: 555.

——. 1947a. The response of normal plant tissues and of crown-gall tumor tissues to synthetic growth hormones. *Amer. J. Bot.*, 34: 53–62.

——. 1947b. The growth-promoting and tumefacient factors of bacteria-free crown-gall tumor tissue. *Amer. J. Bot.*, 34: 248–261.

——. 1947c. Isolation and behavior of bacteria-free crown-gall tissue from primary galls of *Helianthus annus*. *Phytopathology*, 37: 201–206.

——. 1948a. The interaction of normal and crown-gall tumor tissue in in vitro grafts. *Amer. J. Bot.*, 35: 372–377.

——. 1948b. Growth promoting action of bacteria-free crown-gall tumor tissue. *Bull. Torrey bot. Club.*, 75: 45–50.

——. 1948c. Tumor formation on stem fragments in vitro. *Cancer Res.*, 8: 519–530.

——. 1948d. The movement of crown-gall bacteria in isolated stem fragments of sunflower. *Phytopathology*, 38: 993–998.

——. 1948e. Action of streptomycin on plant tumors. *Nature, Lond.*, 162: 459–460.

——. 1949a. The action of antibacterial substances on the growth of *Phytomonas tumefaciens* and of crown-gall tumor tissues. *Phytopathology*, 39: 822–828.

——. 1949b. Inhibitory action of some analogs of folic acid on the growth of plant tumors. *Nature, Lond.*, 164: 954.

——. 1950a. The comparative growth-promoting action of 3-indoleacetic acid and *Agrobacterium tumefaciens*. *Amer. J. Bot.*, 37: 352–363.

——. 1950b. Experimental induction and inhibition of overgrowths in plants. In *Plant Growth Substances* (F. Skoog, ed.), pp. 381–390. U. of Wisc. Press, Madison.

——. 1951a. The growth capacity of the sunflower hypocotyl. *Plant Physiol.*, 26: 778–783.

——. 1951b. The action of some chemical growth inhibitors on healthy and tumor tissue of plants. *Cancer Res.*, 11: 663–668.

——. 1951c. The crown-gall problem. *Bot. Rev.*, 17: 629–670.

——. 1954. The experimental inhibition of the growth of plant tumors. In Symp. on Abnormal and Pathological Plant Growth. *Brookhaven Symp. Biol.*, 6: 128–136.

DIMOND, A. E. 1951. Continuous gamma radiation suppresses crown gall formation in tomatoes. *Phytopathology*, 41: 10.

——, E. M. STODDARD, and S. RICH. 1951. The effect of dyes in retarding the development of crown galls. *Phytopathology*, 41: 911–914.

DUBOIS, K. P., and V. R. POTTER. 1942. Biocatalysts in cancer tissue. I. Cytochrome c. *Cancer Res.*, 2: 290–294.

DUGGAR, B. M., and A. J. RIKER. 1940. The influence of ultraviolet irradiation on the pathogenicity of *Phytomonas tumefaciens*. *Phytopathology*, 30: 6.

DUHAMET, L. 1950. Action du lait de coco sur la croissance des tissus de crown gall de Scorsonère cultivés in vitro. *C.R. Acad. Sci., Paris*, 230: 770–771.

——. 1951a. Action du lait de coco sur la croissance des tissus de crown gall de vigne, de tabac, de Topinambour, et de Scorsonère. *C.R. Soc. Biol., Paris*, 145: 1781–1783.

——. 1951b. Action du lait de coco sur les tissus accoutumés aux heteroauxine de Scorsonère, de tabac, et de vigne. *C.R. Soc. Biol., Paris*, 145: 1783–1785.

——. 1953. Sur la possibilité de survie et de croissance de petits fragments de tissus accoutumés de Scorsonère. *C.R. Soc. Biol., Paris*, 147: 83–85.

DUYFJES, H. G. P. 1935. Het problem der actieve immunizatie van planten tegen *Pseudomonas tumefaciens* Sm. and Town. Thesis, University of Utrecht, Netherlands.

DYE, D. W. 1951. Effects of chemicals and antibiotics on crown gall III. *N. Z. J. Sci. Tech.*, A, 33: 49–54.

——. 1952. Effects of chemicals and antibiotics on crown gall IV. *N. Z. J. Sci. Tech.*, A, 33: 104–108.

——, and P. B. HUTCHINSON. 1950. Effects of chemicals and antibiotic substances on crown gall. II. *N. Z. J. Sci. Tech.*, A, 32: 39–43.

——, ——, and A. HASTINGS. 1950. Effects of chemicals and antibiotic substances on crown gall. I. Colchicine and penicillin. *N. Z. J. Sci. Tech.*, A, 32: 31–39.

EBERTS, F. S., JR., R. H. BURRIS, and A. J. RIKER. 1951. The effects of indole-3-acetic acid and common organic acids on the respiration of slices from tomato stem and crown-gall tissue. *Amer. J. Bot.*, 38: 618–621.

——, ——, and ——. 1954. The metabolism of nitrogenous compounds by sunflower crown gall tissue cultures. *Plant Physiol.*, 29: 1–10.

——, and A. J. RIKER. 1952. Metabolism of nitrogenous compounds by sunflower tissue cultures. *Fed. Proc.*, 11: 206.

ELLIOTT, CHARLOTTE. 1951. *Bacterial Plant Pathogens*. 2nd Ed. Chronica Botanica, Waltham, Mass.

EPHRUSSI-TAYLOR, HARRIETT. 1951. Genetic aspects of transformation in pneumococci. *Cold Spr. Harb. Symp. quant. Biol.*, 16: 445–456.

FARDON, J. C. 1953. A reconsideration of the somatic mutation theory of cancer in the light of some recent developments. *Science*, 117: 441–445.

FEDER, W. A. and P. A. ARK. 1951. Wilt-inducing polysaccharides derived from crown-gall, bean-blight, and soft-rot bacteria. *Phytopathology*, 41: 804–808.

FLINT, L. H., AND C. F. MORELAND. 1945. Note on gall formation in decapitated young bean plants. *Plant Physiol.*, 20: 453–456.

FLINT, THELMA. 1951. The three-dimensional shape of crown-gall cells and a comparison with normal cortical cells of tomato stem. *Amer. J. Bot.*, 38: 342–350.

FLORENZANO, G. 1946. Effect of nitrogenous fertilizers on galls caused on castor-bean plants by *Bacterium tumefaciens*. *Int. Bull. Pl. Prot.*, 20: 11–12.

FRANK, ERICA M., A. J. RIKER, and SARAH L. DYE. 1951. Comparisons of growth by tobacco and sunflower tissue on synthetic media containing various sources of organic nitrogen. *Plant Physiol.*, 26: 258–267.

FRIEDEMAN, B. A., and T. FRANCIS, JR. 1942. Gall formation by *Phytomonas tumefaciens* extract and indoleacetic acid in cultures of tomato roots. *Phytopathology*, 32: 762–772.

FRIEDEMANN, U., and W. MAGNUS. 1915a. Die Tumorbildung an Pflanzen. *Z. Hyg. Infekt Kr.*, 80: 126.

——, and ——. 1915b. Das Vorkommen von Pflanzentumoren erzeugende Bakterien im kranken Menschen. *Ber. dtsch. bot. Ges.*, 33: 96–110.

GAINOR, C., and W. C. PRICE. 1952. Production of galls on *Kalanchoe* by variants of *Agrobacterium tumefaciens* differing in colonial morphology. *Phytopathology*, 42: 8.

——, and ——. 1953. Studies concerning colonial variants of *Agrobacterium tumefaciens*. *Phytopathology*, 43: 509–512.

GARREGUES, R. 1943. Recherches cytologiques sur les tumeurs à *Phytomonas tumefaciens*. *C.R. Acad. Sci., Paris*, 217: 235–237.

GAUMANN, E. 1948. *Pflanzliche Infektionslehre.* Verlag Birkhauser, Basel.

GAUTHERET, R. J. 1946. Comparaison entre l'action de l'acide indoleacétique et celle du *Phytomonas tumefaciens* sur la croissance des tissus végétaux. *C.R. Soc. Biol., Paris*, 140: 169–171.

——. 1947a. Comparaison entre la structure des cultures de tissus normaux et des cultures de tissus de crown gall de Topinambour. *C.R. Soc. Biol., Paris*, 141: 598–601.

——. 1947b. Action de l'acide indoleacétique sur le développement des tissus normaux et des tissus de crown-gall de Topinambour cultivés in vitro. *C.R. Acad. Sci., Paris*, 224: 1728–1730.

——. 1947c. Sur les besoins en hétéro-auxine des cultures de tissus de quelques végétaux. *C.R. Soc. Biol., Paris*, 141: 627–629.

——. 1947d. Plant tissue culture. *Growth Symp.*, 7: 21–43.

——. 1948. Action de l'acide indoleacétique sur le développement de 3 types de tissus de Scorsonère. *C.R. Soc. Biol., Paris*, 142: 774–775.

——. 1952. Remarques sur l'emploi du lait de Coco pour le réalization des cultures de tissus végétaux. *C.R. Acad. Sci., Paris*, 235: 1321–1322.

——. 1952a. Recherches sur l'action combinée de l'hydrazide maleique et de l'acide indoleacétique sur les cultures de tissus de Topinambour. *C.R. Acad. Sci., Paris*, 234: 2218–2221.

——. 1952b. Cancer végétal et culture des tissus. *Rev. Path. comp.*, 52: 100–120.

GENEVES, L. 1946. Investigations sur la formation à deux types cellulaire en crown gall de tomate. *Rev. gén. Bot.*, 53: 381–411.

GHEORGHIU, I. 1932. L'immunité et la vaccinothérapie anticancéreux chez les plantes. *C.R. Soc. Biol., Paris*, 109: 1387–1389.

——. 1938. Les tumeurs expérimentales des plantes causées par divers agents chemiques essai d'explication. *Ann. Inst. Pasteur*, 60: 549–558.

GIOELLI, F. 1940. L'azione di filtrati di *Bacterium tumefaciens* su culture in vitro di tessuti vegetali. *Riv. Pat. Veg., Padova*, 30: 117–130.

GORDON, S. A. 1953. Physiology of hormone action. In *Growth and Differentiation in Plants* (W. E. Loomis, ed.), pp. 273–281. Iowa State College Press, Ames.

——. 1954. Occurrence, formation, and inactivation of auxins. *Annu. Rev. Pl. Physiol.*, 5: 341–378.

——, and R. P. Weber. 1950. The effect of X-radiation on indoleacetic acid and auxin levels in the plant. *Amer. J. Bot.*, 37: 678.

GOSSET, A., A. GUTMANN, G. LAKHOVSKY, and J. MAGROU. 1924. Essais de thérapeutique du "cancer expérimentale des plantes." *C.R. Soc. Biol., Paris*, 91: 626–628.

——, J. MAGROU, and A. TCHAKIRIAN. 1934. Action de divers éléments sur les tumeurs bactériennes du *Pelargonium*. *C.R. Acad. Sci., Paris*, 198: 1096–1100.

HABERLANDT, G. 1921. Wundhormone als Erreger von Zellteilungen. *Beitr. allg. Bot.*, 2: 1–53.

HAMDI, H. 1930. Über die Histogenese, Bau, und Natur des sog. Pflanzenkrebs und dessen Metastasen. *Z. Krebsforsch.*, 30: 547–552.

——. 1932. Über den sog. Pflanzenkrebs und seine Metastasen und ihre Vergleichung mit Tiergewächsen. *Virchows Arch.*, 287: 29–33.

HAMPTON, J. E. 1948. Cure of crown gall with antibiotics. *Phytopathology*, 38: 11–12.

HARVEY, R. B. 1920. Relation of catalase, oxidase, and hydrogen ion concentration to the formation of overgrowths. *Amer. J. Bot.*, 7: 211–221.

HAVAS, L. 1935a. Ascorbic acid and phytocarcinomata. *Nature, Lond.*, 136: 989.

——. 1935b. Follicular (Oestrus) hormone and plant tumors. *Nature, Lond.*, 136: 516.

——. 1936. Some curative effects of mistletoe (*Viscum album*) preparations upon phytocarcinomata caused by *B. tumefaciens*. *Congr. int. Cancer*, 11: 65.

——. 1937. Colchicine "phytocarcinomata" and plant hormones. *Nature, Lond.*, 140: 191.

——. 1939a. Growth of induced plant tumors. *Nature, Lond.*, 143: 789–791.

——. 1939b. Effects of animal hormones and of vitamins on the incremental growth of crown gall. *Congr. int. Microbiol.*, 3: 549–550.

——. 1948. Oncolytic action of some polyploidogenic agents on phytocarcinomata. *Arch. biol. hung.*, 18: 132–144.

——, and A. HEUSNER. 1951. Développement des phytocarcinomes expérimentaux du *Pelargonium zonale* sous l'action de la vitamin K. *C.R. Acad. Sci., Paris*, 232: 2129–2130.

HAYES, L. E. 1946. Survey of higher plants for presence of antibacterial substances. *Bot. Gaz.*, 108: 408–414.

HELLER, R. 1952. Thesis, University of Paris.

HENDERSON, J. H. M., and J. BONNER. 1952. Auxin metabolism in normal and crown-gall tissue of sunflower. *Amer. J. Bot.*, 39: 444–451.

——, MARY E. DURRELL, and J. BONNER. 1952. The culture of normal sunflower stem callus. *Amer. J. Bot.*, 39: 467–473.

HENDRICKSON, A. A., I. L. BALDWIN, and A. J. RIKER. 1934. Studies on certain physiological characters of *Phytomonas tumefaciens*, *Phytomonas rhizogenes*, and *Bacillus radiobacter* II. *J. Bact.*, 28: 597–618.

HENRY, B. W., A. J. RIKER, and B. M. DUGGAR. 1943. Thiamine in crown-gall as measured with the *Phycomyces* assay. *J. agric. Res.*, 67: 89–110.

D'HERELLE, F., and E. PEYRE. 1927. Contribution à l'étude des tumeurs expérimentale. *C.R. Acad. Sci., Paris*, 185: 227–230.

HEYN, A. N. J. 1940. The physiology of cell elongation. *Bot. Rev.*, 6: 515–574.

HILDEBRAND, E. M. 1942. A micrurgical study of crown-gall infection in tomato. *J. agric. Res.*, 65: 45–59.

HILDEBRANDT, A. C. 1950a. Growth of diseased plant tissue in vitro influenced by the concentration of organic acids. *Phytopathology*, 41: 16.

——. 1950b. Some important galls and wilts of plants and the inciting bacteria. *Bact. Rev.*, 14: 259–272.

——, and A. J. RIKER. 1947a. Common alcohols as carbon sources for plant tissue cultures. *Amer. J. Bot.*, 34: 600.

——, and ——. 1947b. Influence of some growth-regulating substances on sunflower and tobacco tissue in vitro. *Amer. J. Bot.*, 34: 421–427.

——, and ——. 1949. The influence of various carbon compounds on the growth of marigold, paris daisy, periwinkle, sunflower and tobacco tissue in vitro. *Amer. J. Bot.*, 36: 74–85.

——, and ——. 1953. Influence of concentrations of sugars and polysaccharides on callus tissue growth in vitro. *Amer. J. Bot.*, 40: 66–76.

——, ——, and B. M. DUGGAR. 1945. Growth in vitro of excised tobacco and sunflower tissue with different temperatures, hydrogen-ion concentrations and amounts of sugar. *Amer. J. Bot.*, 32: 357–361.

——, ——, and ——. 1946a. Influence of crown-gall bacterial products, crown-gall tissue extracts, and yeast extract on growth in vitro of excised tobacco and sunflower tissue. *Cancer Res.*, 6: 368–377.

——, ——, and ——. 1946b. The influence of the composition of the medium on growth in vitro of excised tobacco and sunflower tissue cultures. *Amer. J. Bot.*, 33: 591–597.

——, A. J. RIKER, and JEAN L. WATERTOR. 1952 Growth and virus activity in tobacco tissue cultures with naphthaleneacetic acid or tryptophane. *Phytopathology*, 42: 467.

HILL, J. B. 1928. The migration of *Bacterium tumefaciens* in the tissue of tomato plants. *Phytopathology*, 18: 553–564.

——, W. H. BRITTINGHAM, F. P. GIBBONS, and G. W. WATTS. 1930. Further notes on *Bacterium tumefaciens* and its host relationship. *Phytopathology*, 20: 179–186.

HILL, R. L., and R. C. MILLS. 1954. Lactic dehydrogenase and glycolysis in various microorganisms. *Fed. Proc.*, 13: 229–230.

HORNBOSTEL, W. 1936. Die Beziehungen zwischen Bodenreaktion und Wirkung quecksilberhaltiger Bodenentseuchungsmittel auf den Wurzelkropferreger, *Pseudomonas tumefaciens* Smith und Townsend. *Z. Pflkrankh.*, 49: 77–93.

ISRAILSKY, W. P. 1927. Bakteriophagie und Pflanzenkrebs. *Zbl. Bakt.* (II), 71: 302–311.

IVANOFF, S. S., and A. J. RIKER. 1930. Studies on the movement of the crown-gall organism within the stems of tomato plants. *Phytopathology*, 20: 817–829.

JENSEN, C. O. 1910. Von echten Geschwülsten bei Pflanzen. *Conf. int. Cancer*, 2: 243–254.

——. 1918. Undersgelser vedr rende nogle svulstignende Dannelser hos Planter. *K. VetHøjsk. Aarssk., Kbh.*, 54: 91–143.

JACOBS, W. P. 1952. The role of auxin in differentiation of xylem around a wound. *Amer. J. Bot.*, 39: 301–309.

JOHNSON, J. 1937. Relation of water-soaked tissues to infection by *Bacterium angulatum* and *Bacterium*

tabacum and other organisms. *J. agric. Res.*, 55: 599–618.

JONES, S. G. 1947. An anatomical study of crown-gall tumors on the Himalaya giant blackberry. *Phytopathology*, 37: 613–624.

KAUFFMANN, F. 1928. Zur Tumefaciensfrage. *Z. Krebsforsch.*, 28: 109–120.

——. 1930. Zur biologie der Tumefasciensstämme. *Z. Krebsforsch.*, 30: 290–294.

KENT, G. C. 1937. Some physical, chemical, and biological properties of a specific bacteriophage for *Pseudomonas tumefaciens*. *Phytopathology*, 27: 871–902.

KENT, N. L. 1941. Influence of lithium salts on certain cultivated plants and their parasitic diseases. *Ann. appl. Biol.*, 28: 189–209.

KLEIN, DEANA T., and R. M. KLEIN. 1953. Transmittance of tumor-inducing ability to avirulent crown-gall and related bacteria. *J. Bact.*, 66: 220–228.

KLEIN, G., and E. KEYSSNER. 1932a. Beiträge zum chemismus pflanzlicher Tumoren. I. Stickstoffbilanz. *Biochem. Z.*, 254: 251–255.

——, and ——. 1932b. II. Über die Wasserstoffionen Konzentration in pflanzlichen Tumoren. *Biochem. Z.*, 254: 256–263.

——, and W. ZEISE. 1932. III. Der Katalasegehalt von pflanzlicher Tumoren im vergleich zum Katalasegehalt gesunder Pflanzengewebe. *Biochem. Z.*, 254: 264–285.

——, and ——. 1933. IV. Über Peroxidase in pflanzlichen Tumoren. *Biochem. Z.*, 267: 22–25.

KLEIN, R. M. 1952. Nitrogen and phosphorus fractions, structure, and respiration of normal and crown-gall tissues of tomato. *Plant Physiol.*, 27: 335–354.

——. 1953. The probable chemical nature of crown-gall tumor-inducing principle. *Amer. J. Bot.*, 40: 597–599.

——. 1954. Mechanisms of crown-gall induction. In Symp. on Abnormal and Pathological Plant Growth. *Brookhaven Symp. Biol.*, 6: 97–114.

——, and DEANA T. KLEIN. 1952. Effects of maleic hydrazide on initiation and development of tomato crown-gall tumors. *Amer. J. Bot.*, 39: 727–730.

——, and G. K. K. LINK. 1952. Auxin as a promoting agent in the transformation of normal to tumor cells. *Proc. nat. Acad. Sci. Wash.*, 38: 1066–1072.

——, ELLEN M. RASCH, and H. SWIFT. 1953. Nucleic acids and tumor genesis in broad bean. *Cancer Res.*, 13: 499–502.

KLENKOWSKI, M. 1948. Penicillin und Streptomycin in der Pflanzentherapie. *NachrBl. dtsch. PflSch-Dienst*, 7: 114–117.

KORINEK, J. 1924. Au sujet des agglutinins spécifiques chez les vegetaux. *Publ. Fac. Sci. Carol U.*, pp. 24.

KOSTOFF, D. 1933. Tumor problem in the light of researches on plant tumors and galls and its relation to the problem of mutation. *Protoplasma*, 20: 440–456.

——, and J. KENDALL. 1933. Studies on plant tumors and polyploidy produced by bacteria and other agents. *Arch. Mikrobiol.*, 4: 487–508.

—— and ——. 1945. Origin of a tetraploid shoot from the region of a tumor on tomato. *Science*, 76: 144.

KOVOOR, A. 1953a. Action du jus de Raisin sur la croissance des tissus de crown-gall de Scorsonère cultivés in vitro. *C.R. Acad. Sci., Paris*, 236: 309–311.

——. 1953b. Action stimulante de quelques extraits de fruits et de graines sur le développement de tissus de crown-gall de Scorsonère cultivés in vitro. *C.R. Acad. Sci., Paris*, 237: 271–272.

——. 1953c. Action comparée du liquide intracalicinal de *Spathodea campanulata* Beauv., sur la croissance des cultures de tissus végétaux. *C.R. Acad. Sci., Paris*, 237: 832–834.

KRAUS, E. J., NELLIE A. BROWN, and K. C. HAMNER. 1936. Histological reactions of bean plants to indoleacetic acid. *Bot. Gaz.*, 98: 370–419.

KULESCHA, ZOIA. 1947a. Production de tumeurs par l'inoculation de *P. tumefaciens* dans des fragments de parenchyme vasculaire de Topinambour et de liber de Carrotte cultivés in vitro. *C.R. Soc. Biol., Paris*, 141: 24–25.

——. 1947b. Comparaison entre l'action du *P. tumefaciens* et celle de l'acide indole-acétique sur des fragments de parenchyme vasculaire de Topinambour cultivés in vitro. *C.R. Soc. Biol., Paris*, 141: 232–234.

——. 1947c. Comparaison entre la structure anatomique des neo-formations provoquées par l'action de l'acide indole-acétique et du *P. tumefaciens* sur des fragments de parenchyme vasculaire de Topinambour cultivés in vitro. *C.R. Soc. Biol., Paris*, 141: 358–360.

——. 1949. Recherches sur l'élaboration de substances de croissance par les cultures de tissus de vigne. *C.R. Soc. Biol., Paris*, 143: 1499–1502.

——. 1951. Recherches sur l'élaboration de substances de croissance par les tissus végétaux. Thesis, University of Paris.

——. 1953. Action de l'hydrazide maleique sur la prolifération de tissus de crown-gall de Scorsonère et sur leur teneur en auxine. *C.R. Acad. Sci., Paris*, 236: 958–959.

——, and R. J. GAUTHERET. 1948. Sur l'élaboration des substances de croissance par 3 types de cultures de tissus de *Scorsonère*. *C.R. Acad. Sci., Paris*, 227: 292–294.

KUNKEL, L. O. 1924. Studies on the mosaic of sugar cane. *Bull. Exp. Sta. Hawaii Sugar Planters*, 3: 115–167.

KÜSTER, E. 1915. *Pathologische Pflanzenanatomie.* G. Fischer, Jena.

——. 1926. Regenerationserscheinungen an Bakteriengallen. *Flora*, 120: 179–197.

LAIBACH, F. 1949. Pflanzentumoren und ihre Bedeutung für das Krebsproblem. *Naturw. Rdsch.*, 2: 222–225.

LANCE, C., and R. GAUTHERET. 1952. Sur la pérennité des propriétés tumorales des tissus de crown-gall et des tissus ayant subi le phénomène d'accountumance aux auxine. *C.R. Acad. Sci., Paris*, 235: 1682–1684.

LARSEN, P., and E. BONDE. 1953. Auxin and auxin precursors in plants. *Nature, Lond.*, 171: 180–181.

LASSEUR, P., and M. A. RENAUX. 1935. Research on specific agglutinins in certain plants. *Trav. Lab. Microbiol. Fac. Pharm., Nancy*, 8: 93–107.

LEDERBERG, J. 1952. Cell genetics and hereditary symbiosis. *Physiol. Rev.*, 32: 403–430.

LEE, A. E. 1952. Nitrogen and amino acids in normal, habituated, and bacteria-free crown-gall cultures of grape. *Plant. Physiol.*, 27: 173–178.

LEFEVRE, J. 1938. Sur la présence normale d'acides indoliques et particulièrement de l'acide indol-3-acétique dans diverse plantes supérieures. *C. R. Acad. Sci., Paris*, 206: 1675–1677.

LEVI, I., M. MICHAELIS, and H. HIBBERT. 1943. Studies on plant tumors. IV. Oxidases in normal and tumor beet root tissue. *Arch. Biochem.*, 3: 167–174.

LEVIN, I., and M. LEVINE. 1917. The influence of X-rays on the development of the crown gall. *Proc. Soc. exp. Biol., N. Y.*, 15: 24–25.

——, and ——. 1918a. Malignancy of the crown gall and its analogy to animal cancer. *Proc. Soc. exp. Biol., N. Y.*, 16: 21–22.

——, and ——. 1918b. The biological and clinical evidence of the therapeutic value of radium and Roentgen rays in cancer. *Ann. Surg.*, 37: 443–447.

——, and ——. 1920. Malignancy of the crown-gall and its analogy to animal cancer. *J. Cancer Res.*, 5: 243–260.

——, and ——. 1922a. The role of neoplasia in parasitic diseases of plants. *J. Cancer Res.*, 7: 17–78.

——, and ——. 1922b. The action of buried tubes of radium emanation on neoplasias in plants. *J. Cancer Res.*, 7: 163–170.

LEVINE, M. 1919. Studies on plant cancers. I. The mechanism of the formation of the leafy crown gall. *Bull. Torrey bot. Cl.*, 46: 447–452.

——. 1920. The behavior of crown gall on the rubber tree (*Ficus elastica*). *Proc. Soc. exp. Biol., N. Y.* 7: 157–158.

——. 1921a. II. The behavior of crown gall on the rubber plant. *Mycologia*, 13: 1–11.

——. 1921b. III. The nature of the soil as a determining factor in the health of the beet (*Beta vulgaris*) and its relation to the size and weight of the crown-galls produced by inoculation with *Bacterium tumefaciens*. *Amer. J. Bot.*, 8: 507–525.

——. 1923a. IV. The effects of inoculating various quantities of different dilutions of *Bacterium tumefaciens* into the tobacco plant. *Bull. Torrey bot. Cl.*, 50: 231–243.

——. 1923b. V. Leafy crown-galls on tobacco plants resulting from *Bacterium tumefaciens* inoculations. *Phytopathology*, 13: 107–116.

——. 1924. VI. Further studies on the behavior of crown gall on the rubber plant, *Ficus elastica*. *Mycologia*, 16: 24–29.

——. 1925a. The so-called strands and secondary tumors in the crown-gall disease. *Phytopathology*, 15: 435–451.

——. 1925b. A comparative cytological study of the neoplasms of animals and plants. *J. Cancer Res.*, 9: 11–49.

——. 1925c. Morphological changes in *Bacterium tumefaciens*. *Science*, 62: 424.

——. 1930. The chromosome number in cancer tissue of man, of rodent, of bird, and in crown-gall tissue of plants. *J. Cancer Res.*, 14: 400–425.

——. 1931. Studies on the cytology of cancer. *Amer. J. Cancer*, 15: 1410–1494.

——. 1936a. Studies on *Bacterium tumefaciens* in culture media. *Amer. J. Bot.*, 23: 191–198.

——. 1936b. Plant tumors and their relation to cancer. *Bot. Rev.*, 2: 439–445.

——. 1937. Tumors of tobacco hybrids. *Amer. J. Bot.*, 24: 250–256.

——. 1940. Plant responses to carcinogenic agents and growth substances; their relation to crown-gall and cancer. *Bull. Torrey bot. Cl.*, 67: 199–226.

——. 1947. Crown-gall disease on rhubarb. *Bull. Torrey bot. Cl.*, 74: 115–120.

——. 1950. Bacteria-free plant tumor tissue compared cytologically with tissues influenced by chemical carcinogens grown in vitro. *Amer. J. Bot.*, 37: 664.

——, and E. CHARGAFF. 1937. The response of plants to chemical fractions of *Bacterium tumefaciens*. *Amer. J. Bot.*, 24: 461–472.

LEWIS, D. 1953. Production of polyploids by colchicine and x-rays. *Nature, Lond.*, 167: 891–892.

LINK, G. K. K. 1932. The role of genetics in etiological plant pathology. *Quart. Rev. Biol.*, 7: 127–171.

——. 1933. Etiological phytopathology. *Phytopathology*, 23: 843–862.

——, and VIRGINIA EGGERS. 1941. Hyperauxiny in crown gall of tomato. *Bot. Gaz.*, 103: 87–106.

——, and ——. 1943. Enhanced auxinic activity of

tomato tissues in presence of L-tryptophane. *Bot. Gaz.*, 105: 282–284.

LINK, G. K. K., and D. R. GODDARD. 1951. Oxygen uptake of tomato crown-gall tissues. *Bot. Gaz.*, 113: 185–190.

——, and KATHERINE L. HULL. 1927. Smoothness and roughness and spontaneous agglutination of *Bacterium citri*, *Bact. medicaginis* var. *phaseolicola*, *Bact. phaeoli sojense*, and *Bact. tumefaciens*. *Bot. Gaz.*, 83: 412–419.

——, and R. M. KLEIN. 1951. The terminal oxidase patterns of crown-gall and auxin tumors of tomato. *Bot. Gaz.*, 113: 190–195.

——, ——, and E. S. G. BARRON. 1952. Metabolism of slices of the tomato stem. *J. exp. Bot.*, 3: 216–236.

——, and HAZEL W. WILCOX. 1936. Gall production in high and low carbohydrate tomato plants. *Phytopathology*, 26: 100.

——, and ——. 1937. Tumor production by hormones from *Phytomonas tumefaciens*. *Science*, 86: 126–127.

——, ——, VIRGINIA EGGERS, and R. M. KLEIN. 1953. Role of nitrate-nitrogen nutrition in growth of tomato and crown gall. *Amer. J. Bot.*, 40: 436–444.

——, ——, and ADELINE DES. LINK. 1937. Responses of bean and tomato to *Phytomonas tumefaciens*, *P. tumefaciens* extracts, indoleacetic acid, and wounding. *Bot. Gaz.*, 98: 816–867.

LIORET, C. 1952a. Échanges gazeux respiratoires des tissus de crown-gall de Scorsonère (*Scorsonera hispanica* L.) cultivés in vitro en présence d'acide naphtalene acétique. *C.R. Acad. Sci., Paris*, 234: 237–239.

——. 1952b. Action du "lait de coco" sur les échanges gazeux respiratoires de tissus de crown-gall de Scorsonère (*Scorsonera hispanica* L.) cultivés in vitro. *C.R. Acad. Sci., Paris*, 234: 648–650.

——. 1953a. Action de l'acide α-naphthaleneacétique sur le métabolisme des tissus de racine de Scorsonère cultivés in vitro. I. Accroisement des cultures et variations de constituants azotés et glucidique. *C.R. Acad. Sci., Paris*, 236: 311–313.

——. 1953b. II. Variations des échanges gazeux respiratoires. *C.R. Acad. Sci., Paris*, 236: 504–506.

LOCKE, S. B., A. J. RIKER, and B. M. DUGGAR. 1938. Growth substance and the development of crown gall. *J. agric. Res.*, 57: 21–39.

——, ——, and ——. 1939a. The nature of growth substance originating in crown-gall tissue. *J. agric. Res.*, 59: 535–539.

——, ——, and ——. 1939b. Production of growth substance on peptone broth by crown-gall bacteria and related non-gall forming organisms. *J. agric. Res.*, 59: 525–535.

LONGLEY, B. J., A. J. RIKER, and I. BALDWIN. 1937. Changes in the infective ability of *Rhizobia* and *Phytomonas tumefaciens* induced by culturing on media containing glycine. *J. Bact.*, 33: 29–30.

LOPATIN, M. I. 1939. Influence of bacterial root canker on the development of the cherry tree in the orchard. (Russian). *Pl. Prot., Leningr.*, 18: 167–173.

MAGNUS, W. 1915. Durch Bacterien hervorgerufenen Neubildungen an Pflanzen. *S.B. Ges. naturf. Fr. Berl.*, 7: 263–268.

——. 1918. Wund-callus und Bakterien-Tumoren. *Ber. dtsch. bot. Ges.*, 36: 20–29.

MAGROU, J. 1926a. Sur l'anatomie du cancer des plantes ou crown gall. *C.R. Acad. Sci., Paris*, 183: 986–988.

—. 1926b. Le *Bacterium tumefaciens* dans les tissus du cancer des plantes. *C.R. Acad. Sci., Paris*, 183: 804–807.

——. 1927. Recherches anatomiques et bactériologiques sur le cancer des plantes. *Ann. Inst. Pasteur*, 41: 785–801.

——. 1928. Études sur les galles produites par le *Bacterium tumefaciens*. *Ann. Sci. nat., Bot.* x 10: 545–584.

——. 1935. Réactions d'immunité des plants vis-a-vis du *Bacterium tumefaciens*. *C.R. Acad. Sci., Paris*, 200: 256–258.

——. 1935. Immunité et hypersensibilité du *Pelargonium* vis-a-vis des réinfections par le *Bacterium tumefaciens*. *C.R. Acad. Sci., Paris*, 201: 986–988.

——. 1938. Contribution a l'étude de l'immunité humorale chez les plantes. *Ann. Inst. Pasteur*, 60: 565–600.

——. 1948. *Les Maladies des Vegetaux*. E.F.S. Edition, Paris.

——, and I. LOMINSKI. 1937. Propriétés humorales non-spécifique de certains tissus vegetaux. *C.R. Soc. Biol., Paris*, 125: 224–227.

——, and P. MANIGAULT. 1946. Action du champ magnétique sur le développement des tumeurs expérimentales chez *Pelargonium zonale*. *C.R. Acad. Sci., Paris*, 223: 8–11.

——, and ——. 1947. Action of a magnetic field on crown-gall and on phytopathogenic viruses. *Congr. int. Microbiol.*, 4: 426–427.

MANIGAULT, P. 1953. Étude biochemique des tumeurs du crown-gall chez *Pelargonium zonale*. II. Phosphatase. *Ann. Inst. Pasteur*, 85: 602–620.

——, and J. JUSSIER. 1952. Techniques d'étude de la répartition de la phosphatase au cours du développement des tumeurs expérimentale chez *Pelargonium zonale*. *C.R. Soc. Biol., Paris*, 145: 1788–1790.

MANIL, P. 1953. Action l'antibiotiques sur des tumeurs végétales. *Ann. Soc. Sci. méd. nat. Brux.*, 34: 150–155.

——, and Z. Straszewski. 1950. Effets de l'acide dichlorophenoxyacétique (2,4-D) et de l'acide indoleacétique sur les tumeurs dues à *Phytomonas tumefaciens* Sm. et Town. *C.R. Soc. Biol., Paris*, 144: 311–313.

——, and ——. 1951. Désintegration de *Agrobacterium tumefaciens* par les ultrasons. Absence d'action tumorigène chez les produits obtenus. *Bull. Inst. agron. Gembloux*, 19: 395–398.

——, and ——. 1952a. Action de l'hydrazide maleique sur les tumeurs du crown gall. *Bull. Inst. agron. Gembloux*, 20: 128–131.

——, and ——. 1952b. Action de l'aminopterine (acide 4-amino, pteroylglutamique) sur les tumeurs du crown gall. *Rev. belge Path.*, 22: 96–99.

Marcelli, E. 1950. Carattere endemico dei "tumori radicali" presumibilimenti de *Bacterium tumefaciens* in campi de tobacco. *Notiz. Malatt. Pianti*, 9: 58–60.

McClendon, J. H. 1953. The intercellular localization of enzymes in tobacco leaves. II Cytochrome oxidase. *Amer. J. Bot.*, 40: 260–266.

McEwen, Doris M. 1952. Cancerous response in plants. *Nature, Lond.*, 169: 839.

McKeen, W. E. 1954a. An anatomical study of cane and crown galls. *Canad. J. Bot.*, 32: 527–530.

——. 1954b. A study of cane and crown galls on Vancouver Island and a comparison of the causal organisms. *Phytopathology*, 44: 651–655.

Melhus, I. E., J. H. Muncie, and T. H. Ho. 1924. Measuring water flow interference in certain gall and vascular diseases. *Phytopathology*, 14: 580–584.

Michaelis, M., I. Levi, and H. Hibbert. 1943. Differential inhibitions between normal and tumor (crown-gall) tissues in beet root. *Science*, 98: 89–90.

Milovidov, P. F. 1930. Zur Zytologie der Pflanzentumoren. *Protoplasma*, 10: 294–296.

Mitchell, J. E., R. H. Burris, and A. J. Riker. 1949. Inhibition of respiration in plant tissues by callus stimulating substances and related chemicals. *Amer. J. Bot.*, 36: 368–378.

Montemartini, L. 1938. Il *Bacterium tumefaciens*. *Boll. Ist. sieroter. Milano*, 17: 551–558.

Morel, G. 1948. Recherches sur la culture associée de parasites obligatoires et de tissus végétaux. *Ann. Épiphyt.*, 14: 123–234.

Muncie, J. H., and M. K. Patel. 1929. Potency and specificity of a lytic principle (bacteriophage) obtained from *Pseudomonas tumefaciens*. *Phytopathology*, 19: 98.

——, and ——. 1930. Studies on bacteriophage specific for *Pseudomonas tumefaciens*. *Phytopathology*, 20: 289–305.

Muller, H. 1935. Zur Physiologie von Wund und Krebsgewebe. Thesis, Univ. Greifswald.

Nabelek, V. 1939. Apple exhalation promotes plant tumor. *Z. Krebsforsch.*, 48: 391–399.

Nagy, R., A. J. Riker, and W. H. Peterson. 1937. Comparison of enzymes in crown-gall and non-inoculated plants. *Phytopathology*, 27: 136.

——, ——, and ——. 1938. Some physiological studies of crown gall and contiguous tissue. *J. agric. Res.*, 57: 545–556.

Neish, A. C., and H. Hibbert. 1940. Effect of crown-gall formation on the chemical composition of beets. *Canad. J. Res.*, C, 18: 613–623.

——, and ——. 1943a. Carbohydrate metabolism of normal and tumor tissues of beet root. *Arch. Biochem.*, 3: 141–157.

——, and ——. 1943b. Nitrogen metabolism of normal and tumor tissues of beet root. *Arch. Biochem.*, 3: 159–166.

Nemec, B. 1928. Über Pflanzentumoren. *Ark. exp. Zellforsch.*, 6: 172–177.

——. 1930. Bakterielle Wuchsstoffe. *Ber. disch. bot. Ges.*, 48: 72–74.

Newcomb, E. H. 1951. Effect of auxin on ascorbic oxidase activity in tobacco pith cells. *Proc. Soc. exp. Biol., N. Y.*, 76: 504–509.

Newcomer, E. H. 1951. Mitochondria in plants. II. *Bot. Rev.*, 17: 53–89.

Nitsch, J. P. 1951. Action du jus de Tomate sur la croissance des tissus de crown-gall cultivés in vitro. *C.R. Acad. Sci., Paris*, 233: 1676–1677.

Nobecourt, P. 1928. Contribution a l'étude de l'immunité chez les végétaux. Thesis, Fac. Sci. Lyon, France. Published by Barlier, Tunis.

Noël, Christiane. 1946. Recherches anatomique sur la "crown gall." *Ann. Sci. nat., bot.*, 7: 87–145.

Oppenheimer, H. R. 1926. Verhütung und Heilung krebsartiger Pflanzengeschwülste. *Angew. Bot.*, 8: 8–29.

Paluch, J. 1938. Experiments on the virulence of some strains of *Pseudomonas tumefaciens* and *Phytomonas rhizogenes* and on the influence of some digestive ferments on the experimental crown galls. (Polish). *Acta Bot. Palon.*, 15: 37–46.

Paris, D., and L. Duhamet. 1953. Action d'un mélange d'acides amines et du vitamines sur la prolifération des cultures de tissus de crown gall de Scorsonère; Comparaison avec l'action du lait de Coco. *C.R. Acad. Sci., Paris*, 236: 1690–1692.

Patel, M. K. 1927. Strains of *Pseudomonas tumefaciens*. *Phytopathology*, 17: 46–47.

——. 1928. Strains of *Pseudomonas tumefaciens* and their prevalence in various soils. *Phytopathology*, 18: 129–130.

Patty, F. A. 1930. Some experiments with crown-gall bacteria. *Phytopathology*, 20: 856.

PELCO, J. 1915. Über die Smith'schen Rübentumoren. *Z. Zuckerindust. Böhm.*, 39: 204–219.

PIERI, G. 1953. The action of some antibiotics on *Agrobacterium tumefaciens* and on vegetal tumors. (Italian). *Ann. Sper. Agr.*, 7: 1059–1066.

PINOY, E. 1925. À propos du cancer des plantes ou crowngall. *C.R. Acad. Sci., Paris*, 180: 311–313.

PLATT, R. S. 1954. The inactivation of auxin in normal and tumorous tissues. *Ann. Biol. Paris*, 30: 349–359.

POTTER, V. R., *et al.* 1950. Effects of succinoxidase and oxalacetic acid oxidase. *Cancer Res.*, 10: 28–35.

PRICE, W. C., and C. GAINOR. 1954. Relationship of foliage to stimulation of adventitious roots in crown gall. *Phytopathology*, 44: 107–109.

PURR, A. 1938. Tumoren bei Mensch, Tier, und Pflanze. *Tabul. biol., Hague*, 15: 154–206.

QUIRK, AGNES J. 1931. Smooth and rough colony types at will. *Science*, 74: 461.

RACK, K. 1953. Untersuchungen über die Bedeutung der Verwundung und über die Rolle von Wuchstoffen beim bakteriellen Pflanzenkrebs. *Phytopath. Z.*, 21: 1–44.

REBERT, A. F., and L. J. HAVAS. 1951. Essai de traitement des phytocarcinomes par l'abiotique penitaline. *Rev. Path. vég.*, 30: 25–29.

REDAELLI, P. 1934. Osservasioni su granulomi sperimentali da *Phytomonas tumefaciens* nelli Stapelie. *G. Batt. Immun.*, 7: 1–24.

RIKER, A. J. 1923a. Some relations of the crown-gall organism to its host tissue. *J. agric. Res.*, 25: 119–132.

——. 1923b. Some morphological responses of the host tissue to the crown-gall organism. *J. agric. Res.*, 26: 425–435.

——. 1926. Studies on the influence of some environmental factors on the development of crown gall. *J. agric. Res.*, 32: 83–96.

——. 1927. Cytological studies of crowngall tissue. *Amer. J. Bot.*, 14: 25–37.

——. 1936. Biochemical and physical-chemical studies on the bacteria which stimulate atypical and pathological multiplication of plant cells. *Congr. int. Path. comp.*, 3, I. 2: 107–111.

——. 1939a. The influence of crown gall and hairy root on growth of young apple trees. *Phytopathology*, 29: 21.

——. 1939b. Physiological relations between host and parasite in crown gall—an example of basic biological research with plant material. *Amer. J. Bot.*, 26: 159–162.

——. 1942. The relation of some chemical and physico-chemical factors to the initiation of pathological plant growth. *Growth*, 6: 105–117.

——, and W. M. BANFIELD. 1932. Studies on the development of crown gall, hairy root, and wound overgrowth in the treated soil. *Phytopathology*, 22: 167–177.

——, and T. O. BERGE. 1935. Atypical and pathological multiplication of cells approached through studies on crown gall. *Amer. J. Cancer*, 25: 310–357.

——, and ALICE E. GUTSCHE. 1948. The growth of sunflower tissue in vitro on synthetic media with various organic and inorganic sources of nitrogen. *Amer. J. Bot.*, 35: 227–237.

——, B. W. HENRY, and B. M. DUGGAR. 1941. Growth substance in crown gall as related to time after inoculation, critical temperature, and diffusion. *J. agric. Res.*, 63: 395–405.

——, and E. M. HILDEBRAND. 1934. Seasonal development of hairy-root, crown-gall, and wound overgrowth on apple trees in the nursery. *J. agric. Res.*, 48: 887–912.

——, and A. C. HILDEBRANDT. 1951. Pathological plant growth. *Annu. Rev. Microbiol.*, 5: 223–230.

——, and ——. 1952. Common metabolites and stimulation or inhibition of growth by plant tissue cultures. *Science*, 115: 485.

——, and ——. 1954. Nutrition and diseased plant growths. Symp. on Abnormal and Pathological Plant Growth. *Brookhaven Symp. Biol.*, 6: 79–96.

——, ——, and S. S. IVANOFF. 1932. The development of crown gall, hairy root, and wound overgrowth in glass cylinders. *Phytopathology*, 22: 179–189.

——, ——, and G. W. KEITT. 1930. Seasonal development of crown gall and hairy root. *Phytopathology*, 20: 129.

——, and G. W. KEITT. 1926. Studies of crown gall and wound overgrowth on apple nursery stock. *Phytopathology*, 16: 765–808.

——, M. M. LYNEIS, and S. B. LOCKE. 1941. Comparative physiology of crown-gall, attenuated crown-gall, radiobacter, and hairy-root bacteria. *Phytopathology*, 31: 964–977.

——, J. A. PINCKARD, and I. L. BALDWIN. 1936. Electric potentials found in studies on *Phytomonas tumefaciens* and related organisms and on crown gall. *Phytopathology*, 26: 107.

——, E. SPOERL, and ALICE E. GUTSCHE. 1946. Some comparisons of bacterial plant galls and of their causal agents. *Bot. Rev.*, 12: 57–82.

RIVES, L. 1932. Cancer du plantes et potassium. *C.R. Acad. Agric. Fr.*, 18: 63–67.

ROBERTS, R. H. 1953. A naturally occurring anti-auxin. *Science*, 117: 456–457.

ROBINSON, W., and H. WALKDEN. 1923. A critical study of crown gall. *Ann. Bot.*, 37: 299–324.

ROSE, S. M. 1952. A hierarchy of self-limiting reactions as the basis of cellular differentiation and growth control. *Amer. Nat.*, 86: 337–354.

ROSEN, H. R. 1926. Morphological notes together with some ultrafiltration experiments on the crown-gall pathogen. *Mycologia*, 18: 193–205.

RYBAK, B. 1946. Actions bactériostatique chez *Pelargonium zonale* et crown gall. *C.R. Acad. Sci., Paris*, 223: 586–587.

——. 1947a. Une nouvelle method en microbiologie végétale. *Ann. Inst. Pasteur*, 73: 1015–1023.

——. 1947b. Les problems du crown-gall. *Congr. int. Microbiol.*, 4: 427–428.

——. 1948. Immunité en crown gall. I. *Ann. Inst. Pasteur*, 75: 351–367.

——. 1949. Immunité en crown gall. II. Précisions et fundamental mechanisme. *Ann. Inst. Pasteur*, 77: 688–702.

——. 1953. L'immunité acquise dans le crown-gall. *Congr. int. Microbiol.*, 6: 559.

SAVULESCU, T. 1936. *L'Immunité aux Maladies Bactériennes des Plantes*. Imprimerie Soulisse Marten, Niort.

SCHIFF-GIORGINI, A. 1905. Untersuchungen über die Tuberkelkrankheit des Oelbaumes. *Zbl. Bakt.*, Abt. 2, 15: 200–211.

SCHMIDT, G. W. 1933. Experimentale Untersuchungen über die Entstehung des Pflanzenkrebses. *Schweiz. Z. Hyg.*, 2: 27.

SEGRETAIN, G. Role de la plaie d'inoculation dans le développement des tumeurs à *Agrobacterium tumefaciens*. *C.R. Acad. Sci., Paris*, 228: 1452–1453.

SEMPIO, C. 1935. Influence of cobalt and other cations on the development of experimental tumors by *Phytomonas tumefaciens* on *Ricinus* plants. (Italian). *Atti Soc. ital. Progr. Sci.*, 23 (III): 147–150.

SHERBAKOFF, C. O., and J. A. MCCLINTOCK. 1935. Effect of crown gall, hairy root, and woolly aphids on apple trees in the orchard. *Phytopathology*, 25: 1099–1103.

SIEGLER, E. A. 1928. Studies on the etiology of apple crown gall. *J. agric. Res.*, 37: 301–313.

——. 1929a. Aerial crown gall of the apple. *J. agric. Res.*, 39: 249–262.

——. 1929b. The woolly-knot type of crown gall. *J. agric. Res.*, 39: 427–450.

——. 1930. Effect of the apple strain of the crown-gall organism on root production. *J. agric. Res.*, 40: 747–753.

SKOOG, F. 1935. The effect of X-radiation on auxin and plant growth. *J. cell. comp. Physiol.*, 7: 227–270.

——. 1944. Growth and organ formation in tobacco tissue cultures. *Amer. J. Bot.*, 31: 19–24.

——. 1947. Growth substances in higher plants. *Annu. Rev. Biochem.*, 16: 529–564.

——. 1950. Discussion following paper by P. R. White "Les tumeurs vegetales et le problem de l'etiologie cancéreuse". *Ann. Biol.*, 26: 745–763. 1950.

SMITH, C. O. 1913. Some successful inoculations with the peach crown gall organism and certain observations upon retarded gall formation. *Phytopathology*, 3: 59–60.

——. 1944. A method of inoculating peach seedlings with crown-gall without using punctures. *Phytopathology*, 34: 764–765.

SMITH, E. F. 1911. Crown gall of plants. *Phytopathology*, 1: 7–11.

——. 1912. The staining of *Bacterium tumefaciens* in tissue. *Phytopathology*, 2: 127–128.

——. 1916a. Studies on the crown gall of plants: its relation to human cancer. *J. Cancer Res.*, 1: 231–309.

——. 1916b. Crown gall studies showing changes in plant structures due to a changed stimulus. *J. agric. Res.*, 6: 179–182.

——. 1917a. Embryomas in plants. *Johns Hopk. Hosp. Bull.*, 38: 277–294.

——. 1917b. Mechanism of tumor growth in crown-gall. *J. agric. Res.*, 8: 165–187.

——. 1921. Effect of crowngall inoculation on *Bryophyllum*. *J. agric. Res.*, 21: 593–597.

——. 1922. Appositional growth in crown-gall tumors and in cancers. *J. Cancer Res.*, 7: 1–49.

——. 1923. Twentieth century advances in cancer research. *J. Radiol., Iowa Cy.*, 4: 295–317.

——. 1928. Tumors, cysts, pith bundles, and floral proliferations in *Helianthus*. *Mem. nat. Acad. Sci.*, 22: 1–5.

——, NELLIE A. BROWN, and LUCIA MCCULLOCH. 1912. The structure and development of crown-gall: a plant cancer. *Bull. U. S. Bur. Pl. Ind.*, 255.

——, ——, and C. O. TOWNSEND. 1911. Crown-gall of plants: its cause and remedy. *Bull. U. S. Bur. Pl. Ind.*, 213.

——, and AGNES J. QUIRK. 1926. A begonia immune to crown gall: with observations on other immune or semi-immune plants. *Phytopathology*, 16: 491–508.

SOLACOLU, T., and D. CONSTANTINESCO. 1936. Action de l'acide β-indolyl-acétique sur le développement des plantules. *C.R. Acad. Sci., Paris*, 203: 437–438.

——, and ——. 1939. Action de la colchicine sur les tumeurs par le *Bacillus tumefaciens*. *C.R. Soc. Biol., Paris*, 130: 1148–1150.

SORU, E. 1931. Le potentiel d'oxydo-reduction du tissu sain de la plante (*Pelargonium zonale*) et de la tumeur canceréuse. *C.R. Soc. Biol., Paris*, 106: 415–416.

SPIEGELMAN, S. 1945. The physiology and genetic significance of enzymatic adaptation. *Ann. Mo. bot. Gdn.*, 32: 139–145.

SPIEGELMAN, S. 1946. Nuclear and cytoplasmic factors controlling enzymatic constitution. *Cold Spr. Harb. Symp. quant. Biol.*, 11: 256–277.

——. 1948. Differentiation as the controlled production of unique enzymatic patterns. *Symp. Soc. exp. Biol.*, 2: 286–325.

STAPP, C. 1925. Der Bakterienkrebs der Kartapfeln. I. *Arb. biol. Abt. (Anst.-Reichanst.), Berl.*, 13: 413–418.

——. 1927. Der bakterielle Pflanzenkrebs und seine Beziehungen zum tierschen und menchlichen Krebs. *Ber. dtsch. bot. Ges.*, 45: 480–504.

——. 1935. Contemporary understanding of bacterial plant diseases and their causal organisms. *Bot. Rev.*, 1: 405–425.

——. 1937. Der Pflanzenkrebs und seine Erreger. V. Der Einfluss von T. S.—Hormon (Follikel-Hormon) auf Tumorbildung und Gesamtentwicklung der mit *Pseudomonas tumefaciens* infizierten Wirtspflanzen. *Zbl. Bakt.*, Abt. 2, 96: 81–92.

——. 1939. Bakterielle Pflanzenerkrankungen. *Zbl. Bakt.*, Abt. 1, 144: 94–108.

——. 1943. Der Pflanzenkrebs und seine Erreger. XII. Die Wirkung von Apfelemanation auf Erreger und Wirtspflanze. *Zbl. Bakt.*, Abt. 2, 106: 167–171.

——. 1944. Der Pflanzenkrebs und seine Erreger. XIII. Über die Bedeutung des Colchicins als polyploidesierendes Mittel für den Erreger und als angebliches Bekämpfungsmittel gegen den Wurzelkropfs. *Zbl. Bakt.*, Abt. 2, 106: 338–350.

——. 1947. Der bakterielle Pflanzenkrebs und seine Bedeutung im Lichte allgemeine Krebsforschung. *Naturwissenschaften*, 34: 81–87.

——. 1951. Der Pflanzenkrebs und seine Erreger. XV. Weitere Untersuchungen über Virulenzbeeinflussungen und Bekämpfungsmöglichkeiten. *Phytopath. Z.*, 17: 333–347.

——. 1953. Der derzeitige Stand unserer Kenntnisse über pflanzliche Tumoren. *Zbl. Bakt.*, Abt. 2, 107: 172–189.

——. and H. BORTELS. 1931. Der Pflanzenkrebs und seine Erreger—*Pseudomonas tumefaciens*. I. Konstitution und Tumorbildung der Wirtspflanze. *Z. Parasitenk.*, 3: 654–663.

——, and ——. 1931. Der Pflanzenkrebs und seine Erreger. II. Über den Lebenskreislauf von *Pseudomonas tumefaciens*. *Z. Parasitenk.*, 4: 101–125.

——, and ——. 1933. Der Pflanzenkrebs und seine Erreger. III. Zur Frage der Bekämpfung. *Zbl. Bakt.*, Abt. 2., 88: 313–317.

——, H. MÜLLER, and F. DAME. 1938. Der Pflanzenkrebs und seine Erreger. VII. Untersuchungen über die Möglichkeit einer wirksamer Bekämpfung an Kernobstholzen. *Zbl. Bakt.*, Abt. 2, 99: 210–276.

——, and E. PFEIL. 1939. Der Pflanzenkrebs und seine Erreger. VIII. Zur Biochemie des Krebsgewebes. *Zbl. Bakt.*, Abt. 2, 101: 261–286.

STASNEY, J., A. CANTAROW, and K. G. PASCHKIS. 1952. Production of neoplasms by injection of fractions of mammalian neoplasms. *Ann. N. Y. Acad. Sci.*, 54: 1177–1183.

STRASZEWSKI, Z. and P. MANIL. 1950. Influence de la richesse de l'inoculum et de l'héteroauxine sur la prolifération des tumeurs du "crown-gall." *Ann. Soc. Sci. méd. nat. Brux.*, 3: 169–176.

——, and ——. 1952a. Action, sur le "crown-gall", du filtrat de culture de *Agrobacterium tumefaciens* et d'une suspension bactérienne pure sterilisée à 48°C. *Bull. Inst. agron. Gembloux*, 20: 132–136.

——, and ——. 1952b. Immunité conferée à *Datura stramonium* par une premiere inoculation de *Agrobacterium tumefaciens*; résultats négatifs sur tomate (*Lycopersicon esculentum*). *Bull. Inst. agron. Gembloux*, 20: 387–390.

STRUCKMEYER, B. E. and R. H. ROBERTS. 1955. The inhibition of abnormal cell proliferation with antiauxin. *Amer. J. Bot.*, 42: 401–405.

SUIT, R. F., and E. A. EARDLEY. 1935. Secondary tumor formation on herbaceous hosts induced by *Pseudomonas tumefaciens*. *Sci. Agric.*, 15: 345–357.

SYLWESTER, E. P., and M. C. COUNTRYMAN. 1933. Comparative histological study of crown gall and wound callus on apple. *Amer. J. Bot.*, 20: 328–340.

TATARINOV, M. V. 1937. Experiments on doubling the chromosome set in geranium by means of regeneration. (Russian). *Bull. appl. Bot. Pl.-Breed.*, ser. 15, 2: 79–100.

THEIS, T. N., A. J. RIKER, and O. N. ALLEN. 1950. The destruction of crown-gall bacteria in periwinkle by high temperature with high humidity. *Amer. J. Bot.*, 37: 792–801.

THOMAS, J. E., and A. J. RIKER. 1943. The influence of known chemicals on the initiation of pathological growth and symptoms resembling those of certain viruses. *Phytopathology*, 33: 1119.

——, and ——. 1948. The effects of representative plant growth substances upon attenuated bacterial crown-galls. *Phytopathology*, 38: 26.

THUNG, T. H. 1929. Experimentia met *Baclerium tumefaciens*. *Tijdschr. Plziekt.*, 35: 263–269.

TSAO, T., and W. G. WHALEY. 1950. Uptake and accumulation of phosphorus 32 by normal and gall tissues. *Bull. Torrey bot. Cl.*, 77: 382–384.

VAN LANEN, J. M., I. L. BALDWIN, and A. J. RIKER. 1940. Attenuation of cell stimulating bacteria by specific amino acids. *Science*, 92: 512–513.

——, ——, and ——. 1952. Attenuation of crown-

gall bacteria by cultivation in media containing glycine. *J. Bact.*, 63: 715–722.

——, A. J. Riker, and I. L. Baldwin. 1952. The effect of amino acids and related compounds upon the growth, virulence, and enzyme activity of crown-gall bacteria. *J. Bact.*, 63: 723–734.

Verona, O., and G. Luchetti. 1937. Note sull'azione de alcuni coloranti organici sullo sviluppo di tumori sperimentali de *Bacterium tumefaciens*. *Boll. Fac. Agric. Pisa*, 8: 193–195.

——, and G. Celestri. 1938. The mineral nutrition of plants in relation to their state of soundness. II. Effect of potassium salts on some microbial diseases. (In Italian). *Boll. Fac. Agric. Pisa*, 13: 269–299.

——, and ——. 1938. III. Notes on the action of aluminum on the development of tumors in plants. *Boll. Fac. Agric. Pisa*, 13: 300–303.

——, and ——. 1938. IV. Effect of the chloride and sulfate ions on the development of tumors by *Bacterium tumefaciens* on *Ricinus*. *Boll. Fac. Agric. Pisa*, 13: 458–464.

——, and ——. 1939. Nota sull'azione della ione Al nella sviluppe dei tumori vegetale. *Riv. Biol.*, 27: 19–23.

——. 1942. Nutrizione e virulenza in *Bacterium tumefaciens*. *Riv. Pat. veg., Pavia*, 32: 9–10.

——. 1945. Azione repressiva sullo sviluppo dei tumori dovuti a *Bacterium tumefaciens* dello zolfo somminstrato al terreno. *Ann. Fac. Agr. Pisa*, N. S., 6: 1–7.

Volcani, Z., A. J. Riker, and A. C. Hildebrandt. 1953. Destruction of various tissues in culture by certain bacteria. *Phytopathology*, 43: 92–94.

Waggoner, P. E., and A. E. Dimond. 1952. Crown gall suppression by ionizing radiation. *Amer. J. Bot.*, 39: 679–684.

——, and ——. 1953. Crown gall suppression by anti-auxin. *Science*, 117: 13.

Waksman, S., Elizabeth Bugie, and H. C. Reilly. 1944. Bacteriostatic and bacteriocidal properties of antibiotic substances with specific reference to plant-pathogenic bacteria. *Bull. Torrey bot. Cl.*, 71: 107–121.

Warburg, O., and E. Hiepler. 1952. Versuche mit Ascites Tumorzellen. *Z. Naturforsch.*, 7: 193–194.

White, P. R., and A. C. Braun. 1941. Crown gall production by bacteria-free tumor tissues. *Science*, 94: 239–241.

——, and ——. 1942. A cancerous neoplasm of plants. Autonomous bacteria-free crown-gall tissue. *Cancer Res.*, 2: 597–617.

——. 1945a. Metastatic (graft) tumors of bacteria-free crown galls on *Vinca rosea*. *Amer. J. Bot.*, 32: 237–241.

——. 1945b. Respiratory behavior of bacteria-free crown-gall tissues. *Cancer Res.*, 5: 302–311.

——. 1946. Plant tissue cultures. *Bot. Rev.*, 14: 521–529.

——. 1948. A plant physiologist looks at the cancer problem. *Sci. Mon., Wash.*, 67: 187–192.

——. 1950. Les tumeurs végétales et la problème de l'étiologie cancéreuse. *Ann. Biol., Paris*, 26: 746–761.

——. 1951a. Nutritional requirements of isolated plant tissues and organs. *Annu. Rev. Pl. Physiol.*, 2: 231–244.

——. 1951b. Neoplastic growth in plants. *Quart. Rev. Biol.*, 26: 1–16.

Winge, Ö. 1927. Zytologische Untersuchungen über die Natur maligner Tumoren. I. "Crown gall" der Zuckerrübe. *Z. Zellforsch.*, 6: 397–423.

Woods, M. W., and H. G. DuBuy. 1951. Hereditary and pathogenic nature of mutant mitochondria in *Nepeta*. *J. nat. Cancer Inst.*, 11: 1105–1151.

Wright, S. 1945. Genes as physiological agents. *Amer. Nat.*, 79: 289–301.

NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of Biology. In addition there will occasionally appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to H. B. Glass, Associate Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *Department of Biology, The Johns Hopkins University, Baltimore 18, Maryland, U. S. A.*

"AN EMPIRE OF LEARNING"

—Robert Hooke on China

BY EDWARD H. HUME

The Johns Hopkins University

A Review of SCIENCE AND CIVILISATION IN CHINA. *Volume 1. Introductory Orientations.*

By Joseph Needham; with the research assistance of Wang Ling. Cambridge, at the University Press; [Cambridge University Press, New York]. $10.00. xxxviii + 318 pp. + 13 pl. + 2 folded maps; text ill. 1954.

Here is one of the great books of today, one that puts us all in deep debt to Professor Joseph Needham. It is but the first in a monumental project of seven volumes intended to cover the subject exhaustively. One of the chief attractions in the book is its illustrations, many within the text and a few on the cover.

Here is laid open to us an empire of learning hitherto only superficially understood. We are admitted to converse with the best and greatest minds of the Empire of China, to discover a great mine of treasure, "and make a new Trade to bring it to our shores." We are to learn that the History of Science is more and more widely recognized as an element of supreme importance in the total history of human civilization. Owing partly to circumstances which were bound to bring Europeans into close contact with Indian culture, some justice has been done to the achievements of India, yet the contribution of the Far East, and especially of its oldest and most central civilization, has remained largely clouded and unrecognized. The very term "Far East" indicates an insularity of outlook which all Europeans, though their intentions are of the best, find it difficult to discard. The theme of Joseph Needham's book is the scientific contribution of Asia, and in particular of its "Central Country," China We are to inquire what it was exactly that the Chinese contributed in their several historical periods, ancient and medieval, to the development of scientific thought and technology. How was it that the Chinese ultimately succeeded in forestalling, in many important matters, the scientific and technical discoveries of those who brought about the miracle of Greek thought, and in keeping pace with the Arabs? It is clear that the book uncovers for us many of the empirical discoveries and inventions that affected world history profoundly.

The longer one explores this book, the more is one astonished at the variety of the techniques which Europe adopted from China, generally without any appreciation of their origin, during all the first fourteen centuries of the Christian era. After that, those who ought to have known better failed to give due acknowledgment. As one continues to study Needham's great volume, he discovers what an encyclopedia it is, of language, of pictographs, of symbols, and of phonetics; and what a story it brings us, of the progress of the sciences. Quoting Karlgren, "The literary language has been an artificial thing for a thousand years or more; and for all its stylistic variations it has been essentially the same throughout the ages. Once a Chinese has succeeded in mastering it, it is the same to him, from the linguistic point of view, whether the poem he is reading was written at the time of Christ, a thousand years later, or yesterday; it is just as comprehensible and enjoyable in either case." It is true that this old language, in spite of some ambiguity, has a concentrated, laconic, lapidary quality that makes an impression of austere elegance, pith, and virility, unequalled in any other invented instrument of human communication.

One of the great chapters Needham has given us is entitled Bibliographical Notes. Here we find a record of the books that are truly technological dictionaries. Western scholars have scarcely come to know about

these. Take, for example, the Shih Pên or book of origins, bringing to our attention the names of legendary inventors that include the one who invented arithmetical computations. Most of these inventors are set down as having been ministers of the great Huang Ti, the legendary Yellow Emperor of millenniums ago. On later pages we read of the development of the seed-drill plough; of oilskin rainproof coats; of the establishment of medical officers in every city in the 7th century; of the perfection of dice by Tsao Tzu-Chien; etc. A serious note has to do with the problems of transmission. How did the hodometer and the water-mill appear simultaneously in China and in the Mediterranean area? Did such ideas and techniques appear independently, or in what direction did the ideas travel? We learn that there were things about the Roman Empire that interested the Chinese tremendously and gave them a place in the official histories. There was the significance of jugglers and acrobats, the development of asbestos cloth ("the cloth which can be cleansed by fire—*ho huan pu*"), the night-shining jewel (yeh kuangpi), so fascinating to the Chinese that it was mentioned in all the principal sources. Among the wares of Syrian merchants trading to China were coral and pearls. And important water-clocks came in from the West, not wholly new, for the golden balls, dropping one by one, were a familiar sight.

Needham points out to us one element after another in the body of knowledge that grew up in the Chinese mind, answering to the most rigorous canons of accuracy. Among these elements were historical geographies, edited by such men as Hsü Hsia-k'o, who discovered the true sources of the West River and the Yangtze River. Other elements were plants. The 1406 edition of the *Herbal for the Prevention of Famine* antedated by some seventy years the first European woodcuts of plants. Just a few years later came a learned book describing 541 products used in alchemy. This was followed by *Collected Works on Music and Acoustics*. In this book it was pointed out, several decades before Stevin and Mersenne, what the formula was for the intervals for an equal-tempered musical scale. Undoubtedly the chief scientific achievement of the Ming dynasty (1368–1644 A.D.) was the great pharmacal edited by Li Shih-chen, finished in 1578, and issued in 1596. 1000 plants and 1000 animals are exhaustively described, always with their pharmaceutical values made prominent. There is an appendix giving over 8000 prescriptions. The author provides excellent discussions of distillation, of smallpox inoculation, of the use of mercury, iodine, kaolin, and other therapeutic substances.

It is interesting to note that, after the coming of the Jesuits, "Chinese science fused with universal world science." After that it was no longer easy to distinguish any particular style in the contributions of Chinese thinkers and observers. What the Jesuits began in the 17th century was continued by the Protestants in the 19th century and later. In our own time China has taken her place with all the other nations in a world community of science.

It was in 1606 that Ch'en Ti founded the science of phonology, publishing a work entitled *Investigation on the Sounds in Mao's Version of the Odes*. It was shown that evidence was of two sorts, pên cheng, internal evidence, and p'ang cheng, collateral evidence. About this time there came into being an understanding of philology. During the first years of the 17th century, while Galileo and Kepler and Harvey lived in Europe, in China critical studies began on the *Book of History*. In 1680 the final texts of his philological works were written by Ku Yen-wu, while only seven years later Newton published his *Principia*.

Many have sought to show that much of early Chinese Taoism grew out of Indian Upanishad literature as to its theory, and out of Indian yogism as to some of its practices. Clearly, some of the Taoist schools practiced self-hypnosis by concentration on inhaling and exhaling. In general, it remains clear that the whole atmosphere and intellectual climate of Chinese thought is radically different from either the Indian or the Persian. As to the "Yin-Yang" dualism of Chinese thought, some have suggested that this was an Iranian importation. These words, first used about four centuries B.C., meant "shady side" and "sunny side." After that they suddenly leaped together as philosophical terms. Yin stood for dark, weak, female, etc., while Yang stood for bright, strong, male. It is possible that there was some similarity here to Zoroastrianism, but the influence was unquestionably wholly indirect. Needham agrees with Waley that the aim of the Yin-Yang philosophers was not "the triumph of light," but the attainment in human life of perfect balance between the two principles.

There are paradoxes to note, for example, that the very people who by the nature of their society were prevented from developing a state of society in which iron would have become the basis of the first world-uniting civilization, had mastered the difficult art of iron-casting thirteen centuries before the West. Cast iron was very uncommon in the West before the 14th century A.D. It was certainly practiced on a widespread scale by the Chinese in the 1st century B.C.

About the year 1670 there was a French traveller, François Bernier, physician to the Mogul Emperor Aurungzeb, who was one of the first to appreciate the differences between Asian and Western society. The regulation of the calendar had been, from ancient times, a symbol of submission to the Emperor. Natural phenomena had a "prognosticatory" aspect, scarcely appreciated in the West. Records of sunspots had been kept by the Chinese, who had observed them through thin slices of jade, or some similar translucent material, long before their existence was suspected in the West.

No student of the history of science and civilization should fail to immerse himself in this great book. It belongs to us all. We shall do well to accept and peruse the treasure brought to us so generously.

REVIEWS AND BRIEF NOTICES

General Biology: Philosophy and Education..... 280
Biology: History and Biography..... 281
The Young Naturalist..... 283
Ecology and Natural History..... 283
Evolution..... 284
Genetics and Cytology..... 287
General and Systematic Botany..... 288
Plant Physiology..... 290
Economic Botany..... 291
General and Systematic Zoology..... 292
Animal Growth and Development..... 296
Animal Morphology..... 297
Animal Physiology..... 298
Animal Nutrition..... 302
Biophysics and General Physiology..... 303
Biochemistry..... 305
Microbiology..... 310
Health and Disease..... 311
Psychology and Animal Behavior..... 313
Human Biology..... 324
Biometry..... 328
De Omnibus Rebus et Quibusdam Aliis..... 328

GENERAL BIOLOGY: PHILOSOPHY AND EDUCATION

ALLGEMEINE BIOLOGIE. *Eine Einführung in die Lehre vom Leben. Fourth Edition.*

By Max Hartmann and Hans Bauer. Gustav Fischer Verlag, Stuttgart. DM 56.00. xii + 940 pp.; ill. 1953.

There is in the English language no great, comprehensive work on general biology to compare with this. It comes closer to kinship with the recognized classic of E. B. Wilson, *The Cell in Development and Heredity*, than to any other book, but it exceeds the scope of *The Cell* by including major sections on Metabolism (Stoffwechsel) and Stimulus and Response (Reizerscheinungen). It is enriched by the enormous knowledge of the cellular phenomena of sexual reproduction acquired by its senior author in a lifetime of devotion to that area, and further by the commanding knowledge of genetics and cytology possessed by the junior author, who makes his bow as co-author in the present edition.

The *Allgemeine Biologie* was out of print for a considerable time after the war, much to the regret of those who knew of its excellence and who wished to introduce their English-speaking students to its breadth and comprehensive vision. What other textbook would open with a consideration of the place of biology among the natural sciences, of the methodology of biology, and of the very concept and bounds of *general* biology? Naturally, the first section of the book (63 pp.) deals with the cell, its chemical composition, physical properties, and morphological characteristics. A brief section entitled Statik (29 pp.) follows; it deals with organelles and extracellular products. The third section (93 pp.), entitled Dynamik, deals with the nature and sources of movements. It even includes a brief analysis of the dynamics of bird flight, from von Holst. This is followed by Stoffwechsel (68 pp.).

The interests and abilities of the authors are particularly revealed by the length of the great section entitled Formwechsel (502 pp.). Its major subdivisions are Reproduction, Fertilization and Sexuality, Heredity, Developmental Physiology, and Speciation and Evolution. Particularly the first three of these are considered most fully, and will be most valuable to the careful peruser. Here not only Hartmann's own researches upon the nature of sexuality, but Bělar's magnificent cytological studies, Bauer's researches upon the giant salivary gland chomosomes of the Diptera, the work of Hämmerling on *Acetabularia*, and many other notable modern contributions to biology by German workers, receive their due, although not at the expense of a proper consideration of the advances made in other countries.

The subsections on Developmental Physiology and Evolution, although relatively brief in comparison to the foregoing parts of the section, are nevertheless well balanced and thoroughly modern in point of view. It is interesting to see the work of Kühn and Henke and Holtfreter discussed alongside that of more classical figures such as Wilson, Boveri, and Spemann; and to note the recognition of recent additions to evolutionary theory by Simpson, Rensch, and Dobzhansky.

The section on Reizerscheinungen has also much of interest, but appears not to have been brought up to date so fully as the preceding parts of the book. The work of George Wald on retinal photoreceptors might have received more attention; and the world-renowned work of von Frisch on the responses of bees to polarized light might have gained a place alongside the discussions of the experiments of Hertz on their recognition of shapes.

The final section of the book is frankly philosophical. With the wisdom of age Max Hartmann discusses the Body-Soul Question, the Epistemological Foundations of Biology, Purposiveness and Teleology, and the opposition of Mechanism and Vitalism. The key to his philosophy lies in the following words: "Naturerkenntnis kann eben nur mit der Kategorie der Kausalität

errungen werden; und es gibt keine anderen Methoden, Naturwissenschaft zu treiben, als die Methoden der generalisierenden und exakten Induktion, die Einzelfälle unter allgemeine Gesetzmässigkeit bringen." He has indeed applied that philosophy in writing this great book.

BENTLEY GLASS

BIOLOGY: HISTORY AND BIOGRAPHY

GREEK SCIENCE. *Its Meaning For Us. By Benjamin Farrington. Penguin Books, Melbourne, London, and Baltimore.* 65 cents (paper). 320 pp.; ill. 1953.

This is not a new book, but the occasion of its reprinting in a single Pelican volume, instead of in two, as before, may be made the excuse for some remarks. Let us be quick to admit, in the first place, that Benjamin Farrington is a man of great erudition and that his book is not only readable but is the best available—almost the only—treatise on Greek science. Yet the reader should beware. Farrington is also a writer with a strong Marxist bias, and this has had an obvious influence upon his interpretation of the rise of the scientific outlook among the Greeks. To Farrington, there is little import in that eagerness of mind, that probing curiosity so commonly attributed to the Greeks and recognized by modern scientists as their own primary motive. Like many another socially minded philosopher of science today, Farrington interprets the origins of science as lying in its service to mankind, and as blossoming almost unforeseen from the seeds of utilitarian activities and technologies. His theory seems to be subsumed in these concluding words: "The ancients rigorously organized the logical aspects of science, lifted them out of the body of technical activity in which they had grown or in which they should have found their application, and set them apart from the world of practice and above it. This mischievous separation of the logic from the practice of science was the result of the universal cleavage of society into freeman and slave. This was not good either for practice or for theory."

As a consequence of his own theory, Farrington is at his best in analyzing and discussing the contributions of the more practical men of Greek science, men like Strato and Strabo, Hippocrates, Hero, and Archimedes, and he seems at his weakest in dealing with the men of observation and ideas, such as Democritus and Aristotle. The great Stagirite indeed fares badly, except as to space—he is given an entire chapter. His biological achievements are belittled, for "biology was the preordained field for Aristotle's logic," inasmuch as "nobody was proposing to change plants or animals." Aristotle's ultimate failure is that he *"makes it clear that he regards applied science as something which has already completed its task."* Nothing is said about the Great Scale or Ladder of Beings, nothing about Aristotle's great insight into the nature of animal development or heredity, nothing about his divination of the relationships of the structures of plants and animals to the conditions of their existence, their adaptations. The very word "evolution" is not in the Index—the idea is not discussed at all anywhere; and Xenophanes, whose brilliant deductions about the true nature of fossils and the way in which they come to be preserved were fully 2000 years ahead of his time, is not even numbered among the Greek scientists considered by Farrington. Of course, evolution is not *practical*. On the other hand, Theophrastus, who is usually neglected by historians of science, fares very well here, for Farrington approves of Theophrastus' opposition to the teleology of his master Aristotle, and of his erection of a sharp distinction between plants and animals, inasmuch as it led to a useful separation of botany from zoology.

Farrington's *Greek Science* thus seems at once very stimulating and very biased, excellent in many respects but to be read with a critical mind. Until a better book on the subject comes along—and that may not be soon—it will fill a considerable need for a readable work dealing with the science of the ancient Greeks.

BENTLEY GLASS

SOME ACCOUNT OF THE PENNSYLVANIA HOSPITAL. *Pub. Inst. Hist. Med., 4th Ser. Vol. 4. By Benjamin Franklin; printed in Facsimile, with an Introduction by I. Bernard Cohen. The Johns Hopkins Press, Baltimore.* $3.25. xxxii + 40 pp. 1954.

Following the Reformation and the abolition of Catholic institutions in England, the Church of England apparently abandoned the tradition of maintaining hospitals for the poor. Public almshouses set up infirmaries, but the support of real hospitals devolved upon voluntary, philanthropic groups. After long delay, hospitals so supported were founded in the larger British towns during the mid-eighteenth century; and a similar institution was set up under Quaker auspices in Philadelphia in 1751. Benjamin Franklin was among those who aided in establishing this "Pennsylvania Hospital," and in 1754 he prepared *Some Account* of its founding in order to encourage further contributions for its support. This account was a masterpiece of both prose and printing, but it has long been rare and is now made readily available in the present edition. The text provides a documented analysis of the origins of the first hospital in this country, in the course of which the author remarks on the value of the institution for attending physicians and medical students as well as for the sick poor.

Professor Cohen, in an able Introduction, relates

Franklin's zeal for good works to his puritan background, and comments especially on the latter's indebtedness to the "do good" philosophy of the Reverend Cotton Mather of Boston. Franklin's transplanted New England humanitarianism found a more congenial environment in Philadelphia than might be supposed; since, after all, Puritanism and Quakerism both grew out of much the same English background.

RICHARD H. SHRYOCK

HUMBOLDT. *The Life and Times of Alexander von Humboldt 1769–1859.*

By Helmut de Terra. Alfred A. Knopf, New York. $5.75. xiii + 378 + ix pp., 8 pl., 3 maps. 1955.

"As a reaper of knowledge, there was none among his contemporaries to equal him, for he was thorough and diligent in his studies, whether historical, astronomical, botanical, or geological. He was not content with the gathering of facts and statistical data, but related them to one another, earthquakes with vulcanism and land forms, meteor showers with optical properties of the atmosphere, rock formations with soil types and specific plant associations, climatic phenomena with human behavior." This is Alexander von Humboldt in the words of his most recent biographer, Helmut de Terra. Himself a geologist, de Terra writes interestingly and with keen understanding of Humboldt's early mining career and later fundamental contributions to systematic geology. These facets, though important, are not emphasized at the expense of Humboldt's many other significant activities, of which the most notable is the establishment of the science of plant geography. These accomplishments are skilfully composed against the background of the known aspects of his private life, creating for us a lifelike picture of Humboldt, last of the universal scientists, in his natural habitat, the intellectually explosive terminus of the Eighteenth Century.

Formally, de Terra tells us, Humboldt was educated at Göttingen and the mining academy at Freiburg, but there is truth to the argument that his most profitable textbook was a continent, America. As it did a few years later for Darwin, South America provided many of the challenges which stimulated the development of young Humboldt's philosophy of nature. As he explored and measured his way through the continent, accompanied by the botanist, Bonpland, he gathered much of the material which he was to spend the balance of a long life assembling into an immense collection of writings dedicated to the thesis of the unity of man with the natural universe. Of these, *Cosmos* is his monument, being the unfinished record of his single-handed attempt to create a "portrait of nature."

Humboldt might seem the more interesting to us now, not strictly in terms of facts he wrested from nature, but of his views of the proper uses of our understanding of the universe. Unless it led to the elucidation of the general laws of the universe, he felt the analysis of the minutiae of nature to be useless. As de Terra states his position, "The study of physical phenomena was important only if through them one could listen to an echo from the cosmos." Surely we can learn from such a man.

JAMES F. CASE

CHARLES DARWIN. *A Great Life in Brief.*

By Ruth Moore. Alfred A. Knopf, New York. $2.50. vi + 206 + viii pp. 1955.

The biographies constituting the new Great Lives in Brief series purport to be written "with accuracy, brevity, and clarity." This purpose is fulfilled by Ruth Moore's *Charles Darwin*, which presents a thoroughly satisfactory account of Darwin's accomplishments and an agreeable portrayal of his rather elusive personality. One of Darwin's principal distinctions was the very real skill with which he handled the English language, and though perhaps idle, it is amusing to speculate as to what rank he might have attained as a purely literary figure had the world not focussed its attention on the matter of what he wrote rather than on his style. The author of this biography has shown the good sense to quote liberally from Darwin's own writings, and it is to be hoped that she may lead a number of her readers to his original works and words.

JANE OPPENHEIMER

THE BRITISH CONTRIBUTION TO MEDICINE.

By Jaime Jaramillo-Arango; foreword by Sir Arthur MacNalty. E. & S. Livingstone, Edinburgh and London; [The Williams & Wilkins Company, Baltimore]. $6.00. xii + 220 pp. + 14 pl. 1953.

Dr. Jaime Jaramillo-Arango was a surgeon of distinction in his own land before he became first Minister and then Ambassador of the Republic of Colombia to Great Britain, and his volume, though written originally for Latin Americans, is in English translation a professional as well as a diplomatic tribute to the country in which he spent a number of years. After a brief general survey of the history of British medicine, he has taken up in more detail the British contributions to the conquest of typhoid and paratyphoid fevers, and also of malaria, to the development of penicillin and the antibiotics, to the knowledge of vitamins, and finally to the study of cancer. He does not limit his discussion to British achievements alone, but treats these in relationship to those made in other countries. In devoting special attention, however, to the work of British investigators, he has paid a country which he admires a singularly graceful diplomatic compliment,

and has made a novel contribution to the development of international understanding.

JANE OPPENHEIMER

FRANZ BOAS. *The Science of Man in the Making. By Melville J. Herskovits. Charles Scribner's Sons, New York and London.* $2.50. x + 131 pp. 1953.

Incomparably the leading anthropologist in the United States during his professional lifetime, Franz Boas remains today, more than a decade since his death, still a powerful force. Nothing was more characteristic of the man than his boundless energy harnessed to a profound sense of integrity. It was this that accounted for his enormous production of scientific publications. It was this that made everything he wrote a blow for the truth as he saw it. And it was this that made him so fearless and aggressive a fighter.

Boas entered anthropology at a fortunate moment—for it and for him. Anthropology's potential or even its extent was then unrealized, and for a vigorous, clear thinker like Boas it offered rich opportunities. Anthropology itself benefited profoundly from Boas' insistence on the highest standards of scientific method. His interests were wide and embraced virtually every aspect of this protean subject, but his major efforts were primarily in physical anthropology, linguistics, and cultural anthropology. In all of these he made significant theoretical contributions, many of which are now a part of the foundations of these subjects.

For anyone with Boas' temperament it was inevitable that he would seek a wider audience, especially when he felt that anthropology had something to say on issues of general concern. His forthright and honest comments on race, immigration problems, and other matters that occupied public controversy did much to clarify discussion. And his classic book, *The Mind of Primitive Man*, brought before the general public the generalizations of anthropology, many of which he had a hand in shaping. This, indeed, is the book by which he is known to many people otherwise unacquainted with him. It is a noble monument.

One of the noteworthy characteristics of Boas was his ability to attract students of high caliber and to win their unflagging devotion. This book about him is evidence of that. It was written by one of his former students and breathes a filial spirit. The author, Melville J. Herskovits, a professor of anthropology at Northwestern University, is well qualified to deal with Boas' scientific and intellectual activities. He has touched on most of Boas' principal themes and set them in the perspective of time. His only fault—an amiable one—is a tendency to see no defects in his subject's thinking and to describe him as the very *fons et origo* of almost all of anthropology. His major omission—perhaps an intentional one in a book about a scientific career—is Boas' personal life, which might have thrown added light on the nature of the man. Despite this, Herskovits has done an admirable job, difficult at best, and has pointed up, for anyone to grasp, the significant features of a notable scientist and a seminal thinker.

HARRY L. SHAPIRO

THE YOUNG NATURALIST

HEALTH AND SAFETY FOR YOU.

By Harold S. Diehl and Anita D. Laton. McGraw-Hill Book Company, New York, Toronto, and London. $3.75. xii + 516 pp.; ill. 1954.

Current emphasis on health education at the junior and senior high school level has brought a demand for textbooks oriented to the interests and problems of adolescents. The present volume, which reflects an unusually high degree of authority on the subject from the standpoint of both subject matter and method of presentation, should go far toward meeting this demand.

Beginning with general discussions on the merits of healthful and safe living, the text presents pertinent information about the structure and function of the various organ systems of the body in health and disease, and closes with a consideration of the opportunities for service in the field of health as a vocation. Each of the 28 chapters closes with: (1) a short résumé (under the title, So What?) of the material covered; (2) a list of review questions; and (3) some suggested class activities, entitled Things to Do. Appended are a list of references for further reading on the subject matter of each chapter, a glossary, and a detailed index. Listed also on the copyright page of the volume is a series of motion pictures prepared by McGraw-Hill for use in conjunction with the text.

B. AUBREY SCHNEIDER

ECOLOGY AND NATURAL HISTORY

ASPECTS OF DEEP SEA BIOLOGY.

By N. B. Marshall; illustrated by Olga Marshall. Philosophical Library, New York. $10.00. 380 pp. + 5 pl.; text ill. 1954.

Forty-two years ago there appeared Murray and Hjort's classic, *The Depths of the Ocean*, which throughout four decades has remained the foremost single treatise of its kind. The present volume supplements and, to a great extent, replaces the earlier work. In a prefactory sentence Marshall says, "Mine has not been the almost impossible task of dealing with the whole of a science, but to utilize present knowledge and some of my own unpublished work to build up, chapter by chapter, an integrated account of life in deep oceanic waters."

The book divides naturally into two sections. The

first 5 chapters are concerned with the general aspects of deep sea biology, its growth in the sphere of human knowledge, the means of exploration, the environment, oceanic plants, and deep sea animal life.

The succeeding 8 chapters are in the nature of essays on more or less restricted subjects, all of great interest and elaborated to a most satisfactory degree. It is here that we are conscious, not only of the author's own unpublished material, but especially of the effective methods of synthesis with known facts. Of especial importance are the chapters on counteracting gravity, food chains, sense organs, deep sea sounds and life histories.

The analyses and comparisons of the latter subject provide a vivid impression of the extreme specializations, together with the inexplicable succession of ontogenetic phases of oceanic existence. These are all the more remarkable when we remember that they have evolved in the absence of light and plants and normal surface pressures.

Each chapter has a generous and well-chosen list of references, with indented numbers in the text. An abundance of text cuts and 5 color plates add to the general excellence.

My only criticism is in regard to the makeup of the volume; its excessive weight, its thick, glossy paper, and the very tight binding, all of which contribute a considerable discomfort to the perusal of a most satisfying contribution to deep sea biology.

WILLIAM BEEBE

STREAMS LAKES PONDS.

By Robert E. Coker. The University of North Carolina Press, Chapel Hill. $6.00. xviii + 328 pp. + 16 pl.; text ill. 1954.

This admirable book deals with freshwater communities in general and is a companion of *This Great and Wide Sea*, produced by the same author and publisher in 1947 and 1949. The distinguished author has attempted a difficult task and has succeeded. The subject of freshwater ecology in general, of limnology in its various basic and applied aspects, and the classification, behavior, and distribution of freshwater plants and animals have been reported at length in numerous books, monographs, and technical papers. Robert E. Coker has brought much of this together for the layman in a lucid prose without much loss of technical meaning. No professional background is necessary to enjoy the volume, and a grasp of the importance of freshwaters to man can be obtained by a thoughtful perusal of its contents. On the other hand, the professional limnologist as well as the sanitary engineer will find the book of value. Many important organisms of stream and lake communities are illustrated, as well as their habitats, in a series of simple figures and good photographs.

After an introduction concerned with the value of inland surface waters, there is a section of 7 chapters on water in general, its physical and chemical properties, and its biotic relations. This is followed by a discussion of running water in which small brooklets as well as extensive rivers are considered as dynamic systems. Included is a good chapter on the pollution of streams. The third and last section deals with still water. Ponds and lakes are examined in terms of their inhabitants, ecological relations, and productivity. There is a small but adequate bibliography of about 250 references, with emphasis on the American literature and a good general index.

ORLANDO PARK

THE HUNTING WASP.

By John Crompton. Houghton Mifflin Company, Boston. $3.00. xvi + 240 pp. 1955.

This book is a revised and somewhat rewritten edition of *The Hunting Wasp* that appeared in London in 1948. Regrettably, it has been little improved, and remains a dismaying tract of embarrassing absurdity and sciolistic nonsense. As naturalist, John Crompton seems to have little or no first-hand knowledge of wasps, nor has he evidently benefited by a study of modern publications about them. As author, he seems to be without a sense of accuracy or logic; but his prose simply boils with enthusiasm for his subject. Reweaving, misinterpreting, and floridly rehashing the familiar works of Fabre, the Peckhams, the Raus, and some others, this book has nothing to commend it to one who seeks a popular treatment of the ways of wasps.

From the dust wrapper we learn that *Punch* regards *The Hunting Wasp* as "the most fascinating, vividly lucid book of natural history since Jefferies, or even since Gilbert White." *Punch*, of course, must be allowed its little joke; but, as someone remarked, British humor is not to be laughed at.

KENNETH W. COOPER

EVOLUTION

THE ORIGIN OF LIFE. *Second Edition, with a New Introduction by the Translator.*

By A. I. Oparin; translation with annotations by Sergius Morgulis. Dover Publications, New York. $1.70 (paper); $3.00 (cloth). xxvi + 270 pp.; ill. 1953.

Dover Publications has inaugurated a policy of reprinting some of the rare and scarcely obtainable or very expensive classics of science. *The Origin of Life*, by Oparin, is not an old book, nor is it very rare; but the influence it has already had upon students of evolution is enormous, and the demand must have far

outstripped the supply. Now every serious biology student can acquire his own copy, to stand alongside *The Origin of Species*, which it supplements.

MANUAL FOR HISTORICAL GEOLOGY.

By Percival Robertson. Burgess Publishing Company, Minneapolis. $2.50 (paper). ii + 85 pp., 1 chart, 12 pl.; text ill. 1953.

This, the latest in a number of laboratory manuals in historical geology, has little to distinguish it from its current competitors. The first 5 exercises deal with the study of geologic maps; the arrangement, as stated by the author "is not unusual." These are followed by 8 exercises "dealing with the study of common fossils." In my own experience, the Amphibia and Reptilia, subject of the 8th fossil exercise, hardly qualify as common fossils. There is no exercise on fossil mammals. The arrangement of the others that deal with fossils is somewhat unusual. Trilobites form the subject of the first exercise, while "some Arthropoda other than trilobita, and the hard parts of fish" constitute the 7th, which follows immediately after one on Pennsylvanian plants. The latter is the only one concerned with fossil remains of the plant kingdom. It seems almost certain that the subject matter considered, and its position in the sequence, are based on local opportunities for class field trips, which, the author indicates, are stressed in his presentation of the subject.

The one unusual feature of this manual is the use of a "cut and paste" technique that is reminiscent of early grade-school teaching methodology. The 172 figures on the 12 plates bound in the back of the manual are to be cut out and pasted in appropriate places in the exercises. Regarding this method, the author states:

"No one can find fault with the method of study frequently attributed to Agassiz of requiring the student to draw what he sees. This is undoubtedly the way for the future paleontologist to learn his subject, but the majority of freshmen are not going to be paleontologists and most of them believe that they can't draw. The problem then is to retain and stimulate the natural interest the student has in fossils without decreasing that interest by unnecessary vocabulary and too much drawing. The scheme of cutting out illustrations and pasting them in the proper part of the manual is frankly a compromise. We have not found that the student's interest is decreased by this method and although he does not learn as much as if he had made the drawing, he does learn to identify fossils, and those students who go on into paleontology will have to do the drawing anyway."

While I am inclined to question the value of this method, I am convinced that it would be enhanced by a better selection of illustrative material. Many of the half-tone figures are too dark, others are too light, both defects serving to obscure the significant characteristics of the forms illustrated. Slightly more than half of the 172 figures are line drawings; in general these are not of superior quality.

H. E. VOKES

AN INTRODUCTION TO THE STUDY OF FOSSIL PLANTS.

By John Walton. Adams & Charles Black, London; [The Macmillan Company, New York]. $4.75. x + 202 pp. + 1 pl.; text ill. 1953.

This second edition of John Walton's book follows the excellent standards set in the original edition of 1940. For the area of paleobotany that it covers one can offer only praise. Very few paleobotanists are as well qualified to do this particular job; the text makes clear, concise reading, and the illustrations are pertinent and of splendid quality. Such critical comments as I would care to submit stem, for the most part, from a personal concept of what an introductory treatment on fossil plants should include rather than from any fault in Walton's presentation.

The book deals in large part with Paleozoic petrified plant remains and should be useful for any botany or geology student as an introduction to this area of paleobotanical knowledge. It is obviously not intended as a general reference work nor as a comprehensive textbook suitable for an intensive course in paleobotany. The chapters dealing with the Cordaitales and Coniferales are unduly brief, in view of Florin's monumental contribution to our knowledge of the evolution of the female reproductive structures of this major group of seed plants. That contribution is probably the most significant morphological story that fossil plants have ever revealed and is deserving of a few pages in any general account on plants of the past.

There are a few other groups that might well have been included, such as: the Pentoxyleae, as described by Sahni and his associates, a highly problematical assemblage of plant remains which reveals, in addition to their own unique characteristics, some of the great gaps that exist in our knowledge of the evolution of the plant kingdom; or Frenguelli's interesting *Zuberia*, which might have been included in the account of the Mesozoic Pteridosperms.

It is perhaps justifiable that an author of a textbook should emphasize the areas of knowledge with which he is most intimately acquainted. It is a fact, however, that many writers of paleobotanical texts have ignored, for one reason or another, the fact that far more botanists are interested in the angiosperms than in the vascular cryptogams. Although it seems true that the fossil representatives of the latter group have been less reluctant to yield significant information bearing on their evolution than have the flowering plants, some highly significant and interesting studies have appeared dealing with angiosperm floras in recent decades. I refer to such accounts as Reid and Chandler's *London Clay*

Flora and to the extensive and critically executed works on the Tertiary floras of the western United States, by Chaney, Axelrod, MacGinitie, and others. To include such studies in an introductory account on fossil plants would greatly increase its usefulness. The now rather vast subscience of palynology, in so far as it deals with fossil pollens and spores, also deserves a chapter in any modern paleobotanical text.

The comments offered above suggest my own concepts of what a paleobotanical textbook should include and are not intended as adverse criticisms of Walton's account of the groups he has included.

HENRY N. ANDREW, JR.

BIBLIOGRAPHY OF FOSSIL VERTEBRATES, 1944–1948. *Mem. geol. Soc. Amer., 57.*

By C. L. Camp, S. P. Welles, and Morton Green. Geological Society of America, New York. $5.50. iv + 465 pp. 1953.

This is the fourth volume in its series, which has undertaken to cover the world literature of vertebrate paleontology and paleolithic archeology since 1928. There is first a List of Serials, which supplements those previously given. The Author Catalogue contains approximately 5000 entries, about 1000 more than in the immediately preceding 5-year period, but not yet up to the pre-war record of 7000 entries for 1933–38. There is a Subject Index of 55 pages, a Systematic Index of 160 pages, and a 29-page Synopsis of Classification.

The sight of this superb guide to the literature, now available to vertebrate paleontologists, is enough to turn any biologist green with envy. It is truly astonishing that, with so fine an example before them, the workers in other biological fields have put forth no effort to emulate the example set them. What is lacking? money? initiative? or vision? One thing is certain, the job will have to be done by people who know their science. This is no machine job. Our compliments to Messrs. Camp, Welles, and Green, and to the Geological Society of America.

BENTLEY GLASS

TRIASSIC LIFE OF THE CONNECTICUT VALLEY. *Revised Edition. State Conn. geol. nat. Hist. Surv., Bull. 81.*

By Richard Swann Lull. Connecticut Geological and Natural History Survey, Hartford. $2.00 (paper). 336 pp., ill. 1953.

The handbook since 1915 for students of life during the Triassic period in eastern North America, Professor Lull's monograph now reappears enlarged and revised. As before, it presents a compendium of the ancient vertebrates (chiefly reptiles and reptilian trackways) of the New England Triassic basin, with discussions of the flora and invertebrate fauna and the ecological milieu of 170 million years ago. As a work of synthesis in an increasingly fractionized field, it is truly welcome.

Much of the text remains unchanged, somewhat to the detriment of phases in which important advances have been made. Major innovations include a discussion of the climate and landscape of the Newark epoch as revealed by Krynine's recent studies, analyses of dinosaur footprints by means of dimension graphs and deformation in Cartesian grids, and a series of spirited though hypothetical portraits of the vanished trackmakers. Nomenclature of the reptiles has been modernized. Inclusion of the herbivorous cotylosaur *Hypsognathus* would have helped balance the preponderance of carnivorous forms.

In the Newark beds a dearth of bones is compensated for by a wealth of footprints. On these Lull is the foremost authority, and half the book consists of an illustrated taxonomic review of the form-species. This revision, incidentally, was published almost on the golden anniversary of the author's first monograph on Triassic footprints—a fundamental analysis which established order in a previously confused field. His colleagues may well envy Professor Lull the long and fruitful career of which the *Triassic Life* is the latest testimony.

DONALD BAIRD

MARGINS OF THE SEA.

By Maurice Burton. Harper & Brothers, New York. $3.00. viii + 212 pp.; ill. 1954.

According to the dust jacket, "this book takes the reader on a different kind of excursion along the seashore, not only to observe common forms of marine life but to place them in the long perspective of evolution." Nevertheless, it is quite standard stuff for the most part, except for the chapters on sponges (which are the author's specialty), and occasional patches in which the author digests some recent papers, such as Wilson's on larval settlement. At the outset Burton suggests that catastrophic mortalities may have "contributed to an emergence from the sea, to be followed by a permanent residence." However, this theme is not developed beyond some introductory statements, and most of the space is devoted to familiar problems of evolution in the intertidal environment.

The book is written in the dry British style (as distinguished from what a reviewer in *Nature* calls the "poetic American style"), and shows signs of both careless proofreading and lack of thoughtful revision. Some of the errors are those of syntax or punctuation; others, such as the account of fishing for 7-foot carybdaeid medusae in the Pacific and the statement

by diagram (p. 13) that sea and terrestrial spiders are related, are simply lapses of an author who is perhaps writing too much of this sort of thing.

JOEL W. HEDGPETH

LIVING FOSSILS.

By Maurice Burton; drawings by Jane Burton. Thames & Hudson, London and New York; [Vanguard Press, New York]. $5.00. xiv + 282 pp.; ill. 1954.

This volume is one of a series edited under the title "The Past in the Present," and appears to be presented for the general reader. We must conclude that general readers in Britain have a greater fund of semitechnical and technical information in biological matters than the usual run of readers in America, or that they are willing to go through far more detailed descriptions than is common here. In this country, Burton's book would have greatest appeal to the post-Ph.D. zoologist or paleontologist. It could make the basis for a fascinating series of seminar talks at the graduate level. Indeed, most zoology departments would be delighted to have a man of Burton's turn of mind let his ideas pour forth in an attempt to tie up a subject for the benefit of students and faculty alike.

Specifically, the book deals with living fossils in terms of Osborn's principle of adaptive radiation, and discusses the tuatara, the Stephens Island frog, the platypus and echidna, the world's supply of marsupials, peripatus, *Limulus* and other ancient types of arachnoids, antique crustaceans and insects, the brachiopods, the living coelacanth and early fish, the moas and other ratite birds, and hoofed mammals wherever found. The view is taken that any group of wide and discontinuous distribution, or one whose present numbers is significantly less than in some fossil time, or one whose modern examples are obviously smaller than previous types (as among elephants, sirenians, sloths, and ostriches) is likely to be senile, ready for some combination of factors to erase it—perhaps with an exception or two. Consequently these groups receive careful treatment.

Most of the discussion is based upon the supposed geography of land masses in early geologic time: Gondwanaland from the Cambrian through the Jurassic, with bridges to Laurentia in the lower Carboniferous and to Australasia as late as the Jurassic. The final chapters inquire into the possible causes of extinction and those underlying survival, and cite the information in the literature on monsters and mystery animals.

The whole makes absorbing reading. Ten pages packed with references would have made the book far more valuable to the scientist, and for this audience they could have been spared by an omission of the thumb-nail sketches of anatomy given for modern phyla and classes.

LORUS J. & MARGERY MILNE

GENETICS AND CYTOLOGY

SPECIATION AND VARIATION IN ASEXUAL FUNGI. *Ann. N. Y. Acad. Sci., Vol. 60, Art. 1.*

Edited by Roy Waldo Miner; consulting editor and conference chairman, Kenneth B. Raper; 22 other investigators. The New York Academy of Sciences, New York. $3.50 (paper). Pp. 1–182; ill. 1954.

The proceedings of a conference dealing with such a subject will be read, of course, eagerly and with expectation by all people who are interested both in variation and in fungi. The disappointment will be considerable. It seems almost incredible that at the present date only one of the 14 papers, plus introduction, in this volume, takes any notice of the recent revolutionary advances in the genetics of asexual fungi. These advances started with the pioneer work of Hansen on heterokaryosis and have culminated with the discovery of parasexual recombination in *Penicillium* and *Aspergillus*. If the title of this Conference had been "Variability and Taxonomy," there would be very little to object to. But it was variation: variation is a process and it has to be analysed as a process. At present the only possible approaches to the study of this process are genetics and biochemistry. With few exceptions both are ignored by the contributors.

After having said this, I would like to add that, if one forgets its title, the volume is a very valuable addition to a reference library. A paper by Stauffer and M. P. Backus on *Penicillium chrysogenum* gives an up-to-date summary of the work of the Wisconsin Group. Particularly interesting is a paper by Nickerson on the experimental control of morphogenesis. Five papers deal with variability and taxonomy in the Actinomycetes, some illustrated by beautiful and expensive color plates. A paper by Snyder and Hansen on the Genus *Fusarium* summarizes their admirable spring-cleaning work which has made the taxonomy of this genus manageable also for the non-specialist. Finally, a paper by Dulaney on mutation and selection in some industrially important microorganisms shows a grasp of the implications of modern biochemical genetics which is not obvious in any of the other papers.

G. PONTECORVO

THE GENETICS OF *PARAMECIUM AURELIA*. *Cambridge Monographs in Experimental Biology 2.*

By G. H. Beale. Cambridge University Press, New York. $2.50. xi + 180 pp.; ill. 1954.

The work of Sonneborn and his associates and students has made *Paramecium aurelia* one of the most valuable organisms for studies of cytoplasmic inheritance. Beale, a major contributor to this work, presents the findings in a critical and stimulating fashion. The first two chapters of the book give a background in general genetics and in the special features of the genetics of *Paramecium*. The next three chapters treat in some detail the three types of hereditary transmission upon which the generalizations about cytoplasmic inheritance are based. Each chapter concludes with a critical evaluation of the hypotheses which have been advanced to account for the observations. The discussion of antigen inheritance is especially valuable and includes an original hypothesis not previously advanced. The final chapter summarizes the information for *Paramecium* and puts it together with that from other organisms in a stimulating discussion of cytoplasmic inheritance. The monograph is not a complete compendium of the genetics of *Paramecium* but rather a discussion of cytoplasmic inheritance, this organism being used as a model. As such, it will well repay reading by anyone interested in the basic principles of cellular inheritance.

R. F. KIMBALL

THE GENUS *CLARKIA*. *Univ. Calif. Pub. Bot., Vol. 20, No. 4.*

By Harlan Lewis and Margaret Ensign Lewis. University of California Press, Berkeley and Los Angeles. $2.00 (paper). iv + Pp. 241–392; ill. 1955.

A taxonomic treatment of this western North American genus, a member of the Onagraceae, has become desirable since it has proven itself to be of considerable cytogenetical interest. The major portion of the recent cytological studies has been done by the authors themselves, and these findings, together with taxonomic descriptions, interspecific hybridization problems, and field and garden studies, have been incorporated into the present volume to give a well-rounded treatment of the genus. A considerable number of specific and subspecific changes has been made, to bring the total number of species to 33. Polyploidy, aneuploidy, translocation complexes, and supernumerary chromosomes characterize the genus, but further studies will obviously be necessary to work out the details of species relationships.

PHYSIK UND CHEMIE DES ZELLKERNES. *Protoplasma Monographien, Band 20. Two Volumes.*

By Petr F. Milovidov. Gebrüder Borntraeger, Berlin-Nikolassee. (I) xvi + 529 pp. + 1 pl.; text ill. (II) Pp. 530–664; viii + 479 pp. 1949.

This monograph is exactly what it was meant to be—a valuable reference work of nuclear cytology. The physical and chemical side of this branch of cytology has experienced an extraordinarily active phase in the past decade. No sooner had the type been set, and before Milovidov's original volume, completed in 1940, could be published, than a revision became necessary. To the original 2500 references, a gargantuan bibliography of 1500 fresh publications was added. It would have made for a better book if the publisher would or could have reset the work, so as to put Milovidov's expansions of chapters and paragraphs where they belong. As it is, the scattered addenda have been printed in a separate volume. The result is that the more recent discoveries must be read as a set of footnotes, and to use the book requires constant turning from one volume to the other.

The first, or original, volume is divided into two parts. The topics of Part One include a discussion of theories of mitosis, the optical, electrical, and staining properties of nuclei and their component parts, colloidal and electrolytic properties, viscosity and specific gravity, and the relationship between nucleus and cytoplasm in metabolism. A hundred pages of addenda to these topics are given in Volume Two. Part Two of Volume One concerns mass chemical analysis of nuclear material, on the one hand, and the microspectrophotometric analysis of single cells, on the other. The use of the nucleal reaction in determinations of nucleic acid by this method is criticized and defended. Well over a hundred pages of addenda are given to this section in Volume Two.

Illustrations are scant and poor; the indexing is adequate except for the lack of cross references to the voluminous and important addenda. Clearly publishers of biological monographs of this type would do well to adopt the loose-leaf method so long employed by lawyers, who face, in the unbridled revisions of legislatures, a similar problem.

HUDSON ANSLEY

GENERAL AND SYSTEMATIC BOTANY

LEHRBUCH DER BOTANIK FÜR HOCHSCHULEN.

By Hans Fitting, Richard Harder, Walter Schumacher, and Franz Firbas; (originally by E. Strasburger, F. Noll, H. Schenck, and A. F. W. Schimper). Gustav Fischer Verlag, Stuttgart. DM. 28.00. xii + 651 pp. + 1 folded map; text ill. 1954.

Without attempting at this time to make any major reorganization in this classic among botany textbooks (*Q.R.B.*, 28: 293. 1953), the four authors have endeavored to bring it up to date and to improve the quality of the illustrations, which had deteriorated in the immediate post-war period. Most of the old colored illustrations have been replaced by clearer, fresh

drawings in black and white (but the colored map of plant geographical regions has been retained); and the number of figures has increased by 44.

A glance at the systematic section is enough to show that German botanists are not eager to depart from long-established use by introducing new arrangements and names for the higher categories. The Schizophyta, Thallophyta, Bryophyta, Pteridophyta, and Spermatophyta still reign undisturbed by the ferment that in the United States has erected some 9 or 10 phyla just from the splitting of the Algae alone.

The section on genetics is relatively brief and might have been written twenty years ago. In discussing cytoplasmic inheritance no cognizance has been taken of the illuminating and extensive work on this problem by the authors' compatriot Michaelis. No conspicuous effort has been made to relate genetics to evolutionary processes. Nor is space given to the induction of mutations, gene and chromosomal, by ionizing radiations, ultraviolet, or chemical agents. This section could be signally improved by calling on a plant geneticist for aid.

Probably the paramount use to be made in the United States of this textbook, so far more comprehensive than any which American students are likely to employ, ought to be the diligent consultation of it by prospective authors of botany textbooks in the English language.

BENTLEY GLASS

HOW TO KNOW THE FRESH-WATER ALGAE. *An illustrated key for identifying the more common Fresh-water Algae to genus, with hundreds of species named and pictured and with numerous aids for their study. Pictured-Key Nature Series.*

By G. W. Prescott. Wm. C. Brown Company, Dubuque. $2.75 (cloth); $2.00 (spiral-bound, paper). vi + 211 pp.; ill. 1954.

Here is a very smoothly done, nicely printed, flexible-backed, ring-bound volume ($2.00) which may also be obtained bound in boards ($2.75). There is no question but that this small manual would be of great value to students of freshwater algae anywhere.

An introductory 20-page section of various features gives the essential important elements of phycology for the beginning student. Such topics as the objectives of the book, identification, the pleasures that can be derived from the study of algae, something of their peculiarities, and their classification are covered briefly. The author presents his concepts of the systematics of the algae as 9 phyla: Chlorophyta; Cyanophyta; Chrysophyta; Euglenophyta; Cryptophyta, the cryptomonads or Cryptophyceae of some authors; Pyrrhophyta; Rhodophyta; Chloromonadophyta, a phylum first proposed by Prescott for this very interestingly distinct though small group; and the Phaeophyta. The ecology of the freshwater algae is quickly covered in so far as its more outstanding and some of its more novel features are concerned, in 5 pages that include methods of collecting and preserving. This is followed by 2 pages listing the most desirable literature.

The body and meat of the text follows as an extensively illustrated, practical key to the genera of freshwater algae. While as a rule the phyla are keyed out in lumps, such academically nice arrangements have not bound the author in his attempts to make the volume useful. As an example, *Vaucheria* is keyed out near *Dichotomosiphon*, among the green algae. In so doing Prescott makes the clear statement that this practical arrangement does not mean that *Vaucheria* is anything other than a heterokont alga belonging to the Chrysophyta. While there are only occasional notes as to the species to be found, there are often notes on the ecology and other interesting features of species of the genus. That this is not just another key to a state flora is clear from the non-geographically restricted generic ecology and check list of more common genera.

There is no doubt that the author is the most active authority on freshwater algal floristics today. This is shown in many places in his textual treatment, for example, in his skilfully designed and executed illustrations which, whether for interest as in the introductory sections of the book, or for purposes of identification as in the illustrated key, are artistically pleasing and add greatly to the volume's appearance.

The field of freshwater phycology is one of those in the botanical area which is most lacking in adherents to the principles of priority and the type method. Prescott, though undoubtedly one of the men best qualified to follow such procedures, seems to advise against it or even to ridicule such principles. His ostensible position or excuse may be quoted from the Introduction, where he writes: "The generic names used in the key are those of long-standing and the ones to be found in floras and handbooks the world over. In a few instances the names have been reduced to synonymy by specialists who have critically examined the old taxonomic literature for long forgotten synonymies. The advanced student is urged to look into the writings of specialists if he wishes to adopt the recent taxonomic terminologies." At best this is a "loaded" statement. Certainly, the advanced scientific student should also be permitted to know that neither "common belief" nor "might" make right, and that in science priority is what is recognized as right when one has two names to choose between and that the type method is the way one tells to which genus a generic name belongs. Furthermore the *advanced* student of algae should, rather than accept the writings of an authority, be encouraged to determine for himself the correct name to use.

The usefulness of this volume is greatly enhanced by one still unmentioned feature, the Index and Pictured-

Glossary. In it not only are page references given to names, but terms are defined *and illustrated*. Such features lead the reviewer to recommend enthusiastically this novel aid to identification of the algae, either for use as a class text or as a guide for independent study, or to the more advanced student just for the notes included from the author's vast experience with freshwater algae.

MAXWELL S. DOTY

HANDBOOK OF ALGAE *with Special Reference to Tennessee and the Southeastern United States. Contr. Bot. Lab. Univ. Tenn., N. Ser. No. 155.*

By Herman Silva Forest. The University of Tennessee Press, Knoxville. $4.75. vi + 467 pp. + 2 maps; ill. 1954.

This attractively bound gold and blue volume represents a normal extension of its author's previous check lists and literature studies of the algae of what he refers to as the Tennessee region. This area comprises essentially the watersheds of the rivers draining Tennessee. Forest has divided his geographic area into ten subdivisions based largely on the physiography coincident with soil types and to a lesser degree with terrestrial vegetation.

An extensive key to the genera is the initial section of the book. This is dichotomous, with alternating pairs of choices indented in the typography, and most desirable for taxonomic use when a key of such length and students are concerned. Adherence to the standard dictionaries, so as to eliminate such words as "septating," would have been desirable. There is a page and a half glossary defining technical terms, and this is, of course, a desirable feature. However, in the glossary appear various oddnesses, e.g., "hormogone," a mutilation of the word "hormogonium," which is the form used in the text, at least as "hormogonia."

The generic key makes no reference to the systematic treatment of each genus. Thus when one "keys out" a specimen he then looks up the page in the index and then turns to the genus in question. From experience with student keying there is usually found more than one tentative answer and this necessary search for the descriptions and figures is bound to depreciate the student's success.

The groups of algae are taken up in a systematic arrangement, with descriptions of each species and genus and at least one illustration for each genus. A seemingly very desirable feature of this book is the illustration, as well, of the author's concept of almost each species. The line figures themselves are often relatively crude, but with each species there are listed several literature treatments, and these papers are cited in the bibliography.

As an extensive annotated treatment of the fresh water algae of Tennessee, this photolithed volume takes its place along with the very few state algal floras we have. As a guide to the algae it will undoubtedly be of great use to students interested in that area.

MAXWELL S. DOTY

FIELD BOOK OF AMERICAN WILD FLOWERS.

By F. Schuyler Mathews; completely revised and enlarged by Norman Taylor. G. P. Putnam's Sons, New York. $5.00. xxx + 601 pp.; ill. 1955.

Since it was first published over a half century ago, this book has been the most satisfactory guide we have to our herbaceous wild flora. The present enlarged edition, making use of revisions incorporated into the recent Gray's *Manual*, maintains the same high standards of coverage, clarity, and illustration. Any field naturalist or enthusiast will be the poorer if he lacks this excellent and convenient-sized volume.

PLANT PHYSIOLOGY

AUXINS AND PLANT GROWTH.

By A. Carl Leopold. University of California Press, Berkeley and Los Angeles. $5.00. xii + 354 pp.; ill. 1955.

Auxins and Plant Growth, by A. C. Leopold, is a useful, timely, and well-organized presentation of the major aspects of the physiology of the plant growth hormone. It includes chapters on the practical applications of auxins in agriculture, and goes into some detail regarding dosages and effective compounds for different crops, as well as the rationale of their use. The first half of the book is devoted to the theoretical background of auxin physiology. As an introduction to the field for horticulturalists who will be using these materials, or as supplementary reading for a course in plant physiology, this should be a valuable and easily read book. Quite useful, also, are the specific instructions for all the auxin bioassays.

The weakest aspect of the book is its interpretation of the processes of plant growth and development. The general impression that the book leaves is that a particular growth process is understood, if once we know what (low molecular weight, soluble) chemicals can alter, control or initiate the process. For instance, Leopold reviews the recent work of Skoog and his coworkers on the effects of adenine and auxin on differentiation, and then concludes: ". . . the concentration ratio of auxin to adenine will determine to a large extent whether buds, callus or roots will be formed" (p. 105). This is certainly true as far as it goes, but it is certainly only the very beginning of the story. There is no idea yet of what role adenine is playing in these plant tissues (tobacco stem segments) in which it is required for bud initiation, etc.; whether it is most

limiting for nucleic acid synthesis or formation of pyridine nucleotides or ATP or other cofactors; what the nature of the interaction with auxin involves; what other soluble cofactors are actually involved but are not seen because the tissue synthesizes enough for itself; which half dozen or hundred enzymes are required for the overall process; how orientation of growth is achieved to form the proper patterns; etc., etc. Although it would not be appropriate to include a large amount of speculation in a book of this sort, it would have been a good idea to give some hint that present understanding is just barely scratching the surface of a complex problem.

Another example of this simplifying orientation is found in the discussion of accessory organic nitrogen compounds required, together with auxin, for rooting (p. 205). Various workers have reported the following compounds to be effective in this regard, in different plants: arginine, adenine, biotin. Leopold's comment is: "It is entirely possible that the most effective form of soluble nitrogen varies from one species of plant to another." This comment implies that all three chemicals are performing equivalent functions, and the difference between them is merely in ease of assimilation. However, considering the diverse nature of the compounds and the different dose levels for effectiveness, it is very questionable to put them all in the same category. It seems much more reasonable to assume that the initiation of roots, although a single physiological fact, requires the participation of many biochemical activities; different species may then be limited in their ability to synthesize any of the cofactors for each of the biochemical processes in turn, and so each plant will root only when its particular need is met. Instead of sketching some such complex biochemical background for the physiological activity, *Auxins and Plant Growth* leaves us with the picture that the process of rooting involves giving a plant tissue a lot of auxin, not too much adenine, enough carbohydrates, and extra soluble nitrogen.

Again, branching in roots and in stems is compared on the same level. Branching in stems, according to *Auxins and Plant Growth*, is caused by a lack of inhibiting auxin from the tip; branching in roots is caused by the same thing, but other (unspecified) factors may be involved (p. 101). This is essentially all that is said about the two processes. However, it seems almost superficial to fail to mention, at this point in the book, that branching in stems results when lateral buds, already present, are released from an auxin inhibition; whereas in roots branches are adventitious, and the process of branching involves first and foremost the initiation of new meristems.

There are many other instances throughout the book where the discussion of a particular phenomenon is adequate as far as it goes, but stops short of pointing out the full implications as to the mechanism underlying the phenomenon. That this is not a necessary failing of a work of this sort can be seen from reading *Plant Growth Substances*, by Audus, a similar book published recently.

In spite of these over-simplifications in regard to the larger problems, *Auxins and Plant Growth* does not leave one with the impression that everything is perfectly understood and further research is unnecessary. Many interesting speculations and unexplained details are presented concerning the facts of auxin physiology proper—such as changes in auxin or inhibitor levels, the only partial correlations with other phenomena such as flowering, etc. These sections should serve to stimulate and orient future research.

Taken as a restricted work, then, *Auxins and Plant Growth* is an excellent book. It covers a very large amount of material and organizes it into a coherent picture on the theoretical side; and it presents the rationale behind most of the present-day practical uses of auxins in agriculture. The one reservation about it being clearly recognized, the book should be a valuable addition to an advanced course in physiology or plant growth and development. It will be extremely useful for workers in applied research.

A. T. JAGENDORF

ECONOMIC BOTANY

WEEDS. *Second Edition.*

By Walter Conrad Muenscher. The Macmillan Company, New York. $10.00. xvi + 560 pp.; ill. 1955.

This is the second edition, brought up to date, of a book that has been most useful, and has enjoyed a wide reputation for clarity and accuracy. It differs from its predecessor only in the addition of descriptions of plants that have assumed a weedy character in the last twenty years, some new plates, and more modern methods of control. The keys are workable, the illustrations clean, and the descriptions adequate. The cost is unfortunately high, but it remains the only satisfactory book of its kind in this country.

PRIMROSES AND POLYANTHUS.

By Roy Genders and H. C. Taylor. Criterion Books, New York. $3.00. 143 pp. + 16 pl. 1954.

The primroses and their relatives are experiencing a reviving popularity after being on the decline for many years. These were popular flowers in the reign of the Tudors, but lost out to the more recent introductions with the passing years and changing fads. Yet as every flower sooner or later finds a champion, so has the primrose, and the present volume deals in most delightful fashion with its history, types, and cultivation. The primrose is, of course, peculiarly English,

and few places in America, with the possible exception of the cool and moist Northwest, can grow these plants to the perfection that the English gardener can; but the species and varieties are sufficiently varied in form and soil preference to be worthy of trial by anyone who has a suitable spot in his garden. This is a book that does full justice to a most worthy subject.

C. P. SWANSON

VEGETABLE AND FLOWER SEED PRODUCTION.
By Leslie R. Hawthorn and Leonard H. Pollard. The Blakiston Company, New York and Toronto. $7.50. xiv + 626 pp.; ill. 1954.

This work offers a very complete and comprehensive treatment of this important aspect of agriculture and industry. At the time it was written there was no other text devoted exclusively to this subject. However, references to seed production appear throughout the literature, and Hawthorn and Pollard have done excellently in bringing all of this information together in a modern text. The authors pay proper respect to David Landreth, the first American seedsman, whose picture makes the frontispiece.

The 600-page volume is composed of four parts. Part I deals with the seed industry as a whole. It includes a history of the industry in the United States, as well as a discussion of plant breeding and environmental factors related to seed production. The proper cultural methods for producing vegetable and flower seeds are not discussed in detail, because the same cultural techniques that apply to the marketable crops are applicable to seed production. Since there are many excellent recently published texts dealing with crop production, the authors refer the reader to them. The authors quote liberally from many of the publications they cite.

Part II, which is approximately 400 pages in length, deals with vegetable seed crops and is comprised of separate chapters on such families as the Umbelliferae, Liliaceae, Compositae, Cucurbitaceae, Gramineae, Leguminosae, Cruciferae, Chenopodiaceae, and Solanaceae. Each chapter touches on the diseases and insects that affect the crop and the methods of control, plant characters, breeding methods of seed production, roguing, fertilizers, weed control, methods of seed harvesting, threshing, storage, etc.

Part III deals with the growing of flower seeds. The flower-seed industry, in contrast with the vegetable-seed industry, is rather small, and amounts to approximately 3% of the latter. The bulk of the flower seed produced in the United States is produced by five major seed companies, each of which markets more than $100,000 worth of flower seeds annually. The principal flower-seed crops are the sweet pea, zinnia, aster, stock, nasturtium, and petunia. The treatment of flower-seed production is not as detailed as that of vegetable-seed production. Approximately 25 annuals and 10 perennials or biennials are discussed.

Part IV deals with harvesting and milling equipment, seed storage, and the handling and marketing of seed.

The authors have compiled a great deal of useful information and have presented it in a very interesting manner. The textbook should be valuable to university and extension personnel as well as to farmers engaged in seed production.

C. E. MINARIK

GENERAL AND SYSTEMATIC ZOOLOGY

GRUNDRISS DER ALLGEMEINEN ZOOLOGIE.
By Alfred Kühn. Georg Thieme Verlag, Stuttgart; [Intercontinental Medical Book Corporation, New York]. DM 16.50. vii + 281 pp.; ill. 1955.

The eleventh edition of Kühn's *Grundriss* differs in only minor details from the tenth, issued in 1947 (*Q.R.B.*, 27: 94. 1952), which represented a more extensive revision of previous ones. Kühn's texts on general biology are by now so well known and so highly respected that they require little recommendation, yet it is always a pleasure to note their appearance in continually improving guise. The review of the tenth edition of the *Grundriss* called attention to the usefulness of the volume for students who wish to enrich their knowledge of German as well as of zoology. The point about language is that it is clear in measure as the thought it wishes to express is clear. Kühn's volume is a model of clarity and incisiveness because of the remarkable qualities of Kühn's mind, which is one of the most masterful now functioning in its ability to fit fact and detail into a framework of fundamental principles. This book, like his others, is recommended in the strongest possible terms to all who are interested in the basic problems of the animal organism.

JANE OPPENHEIMER

INSTRUCTIONS FOR COLLECTORS. *2nd Edition. Invertebrate Animals Other Than Insects. No. 9A.*
British Museum (Natural History) London. 3s. 6d. iv + 76 pp. + 12 pl.; text ill. 1954.

The British Museum of Natural History has here published a very useful small handbook containing authoritative information on the collection and preservation of invertebrates other than insects. An introductory section explains with the aid of plates how to distinguish the various groups of invertebrates. This is followed by specific directions for securing and preserving the various groups; and a final part deals with

equipment, chemicals, and handling of collections. The handbook should be useful even to experienced zoologists.

L. H. HYMAN

LEHRBUCH DER SPEZIELLEN ZOOLOGIE. *Teil I: Wirbellose. 1. Lieferung.*

By Alfred Kaestner; with the collaboration (Section Protozoa) of Arno Wetzel. Gustav Fischer Verlag, Jena. DM 11.30 (paper). xii + 220 pp.; ill. 1954.

This first part of a college text of zoology carries the invertebrates from the Protozoa through the aschelminth worms. The scheme of classification adopted is conservative, yet recognizes modern trends such as the division of the Bilateria into Protostomia and Deuterostomia, although Cnidaria and Ctenophora are united under the name Coelenterata. The treatment is mainly morphological, although a small amount of ecological information is included. Each group is given a general treatment, well illustrated by naturalistic black-and-white figures, some traditional, others less usual.

L. H. HYMAN

BATHYPELAGIC NEMERTEANS OF THE PACIFIC OCEAN. *Bull. Scripps Instn. Oceanogr., Vol. 6, No. 7.*

By Wesley R. Coe. University of California Press, Berkeley and Los Angeles. 75 cents (paper). i + pp. 225–286; ill. 1954.

The collections from recent expeditions of the Scripps Institution of Oceanography and from the biological survey of the great submarine canyon at the entrance to Monterey Bay by the personnel of the Hopkins Marine Station have increased the number of deep-sea nemerteans known to occur in the Pacific Ocean to 29 species, in a world total of 67. In this publication the world's leading authority on these worms, which live at depths from 500 to 2000 meters or more, describes and figures each of the 29 Pacific species, of which 7 were previously known only from the Atlantic Ocean, and 10, representing 4 new genera, are previously undescribed species. The geographical distribution of each species is also described. Very little is known of the biology of these nemerteans, beyond what may be deduced from their anatomy.

INTRODUCING SEASHELLS. *A Colorful Guide for the Beginning Collector.*

By R. Tucker Abbott; illustrated by Frederick M. Bayer. D. Van Nostrand Company, Toronto, New York, and London. $2.50 (paper). vi + 64 pp. + 8 pl.; text ill. 1955.

R. Tucker Abbott, author of the recently published, and very excellent, *American Seashells* has prepared a short "guide for the beginning collector" that is largely paraphrased from the more extensive work. The 4 color plates and the color illustrations forming the front and back covers are all taken from the previous book, like the majority of text figures. Added are 4 plates of artistic black-and-white photographs that mainly depict tropical Indo-Pacific species.

The chapter titles—Introducing Seashells; Hunting Your Own Shells; Exploring our Color Plates; Preparing Shells for the Collection; Strange Seashells; A Collector's List of Shell Names; and Dealers and Clubs—indicate the scope of the material discussed. There is much here that will be of interest to the advanced collector as well as to the beginner, but the treatment is so generally abbreviated as to make me feel that it falls far short of its announced purpose as a "guide."

H. E. VOKES

A MANUAL OF THE DRAGONFLIES OF NORTH AMERICA (ANISOPTERA) *including the Greater Antilles and the Provinces of the Mexican Border.*

By James G. Needham and Minter J. Westfall, Jr. University of California Press, Berkeley and Los Angeles. $12.50. xii + 615 pp. + 1 pl.; text ill. 1955.

Beginners and experts have here the means of identifying the adults and all known nymphs of the 332 species of dragonflies (Order Odonata, Suborder Anisoptera) which are to be found on this continent. Part I, 58 pages in length, includes a characterization of the order, a general description of the external anatomy, a few notes on habit and habitat, detailed directions to the beginner for collecting and preserving specimens, and a brief bibliography of the most frequently cited references. Part II includes keys and tables to families, subfamilies, genera, and species, and a description of each species. Each genus is illustrated by line drawings or photographs which show the wing venation of the adult and the general conformity of the nymph. Most species are accompanied by photographs of the genitalia.

One notes the absence of any mention of subspecific categories, the paucity of field and ecological notes, and the lack of detailed information about metamorphoses. But the authors state that this book is "first of all a means of finding the names of dragonflies" and that any student of the group will need the senior author's *Handbook of Dragonflies*, even though much of the material in that book is included in this one. In their first objective the authors are eminently successful, for this is an excellent manual for species

identification. The lack of page references in the keys and of figure references in the text detracts considerably from its usability, however.

The junior author's technical skills have been superbly applied in preparing the illustrations. His photographs of genitalia and of nymphs are superior to anything hitherto published in this field.

ELSIE B. KLOTS

THE HORSE-FLIES (DIPTERA: TABANIDAE) OF THE ETHIOPIAN REGION. *Volume II. Tabanus and related genera.*

By H. Oldroyd. British Museum (Natural History), London. £2. 10s. x + 342 pp. + 5 pl.; text ill. 1954.

The second volume of Oldroyd's *Ethiopian Horse-flies* follows the same excellent style and comprehensive treatment established in the first one (*Q.R.B.*, 29: 170. 1954). The Tabanini is better known than the group previously treated, though smaller in total number of species. As a consequence the author, following the trend of workers in the same family but in other regions, has divided the 130 previously known and 17 new species into 10 genera (3 new), 5 subgenera (2 new), 6 species-groups and 2 other groups based on abdominal pattern which are subdivided into 3 and 7 subgroups. Copious and well-drawn illustrations, many by the author, supplement the keys and should make them more useful to non-specialists.

A comprehensive section on the biology of the horse-flies, including their early stages, the food of adults, and their transmission of diseases, is included. The section on geographical distribution will be of much interest to those interested in the life-zones of the Ethiopian region.

FRED M. SNYDER

ASCIDIANS OF SAGAMI BAY *Collected by His Majesty The Emperor of Japan.*

Described and illustrated by Takasi Tokioka; edited by Hirotaro Hattori. Iwanami Shoten, Tokyo. Y. 2500. x + 316 pp. + 79 pl. + 1 map; text ill. 1953.

Tokioka has here done a splendid piece of systematic work that will be indispensable to all students of tunicates. Introductory sections on the general structure of ascidians are in Japanese, but the taxonomic descriptions are repeated in English. Of 112 species of tunicates recorded from Sagami Bay, 81 are here described and illustrated, including 21 new species and 3 new forms. The illustrations are of the usual high artistic quality typical of the Japanese.

L. H. HYMAN

AN INTRODUCTION TO ORNITHOLOGY.

By George J. Wallace. The Macmillan Company, New York. $6.00. xii + 443 pp.; ill. 1955.

Although I do not know too much about the publishing business, nevertheless it has always seemed to me that a book suitable for college bird courses would be a worthwhile publication. For many years I have complained to visiting book salesmen that in spite of the tremendous number of books that have been written dealing with birds, there was nothing that could be used as a textbook. As a matter of fact, I had even started to write one. Fortunately I am now spared that ordeal. The present book, written by a well-known and respected member of the profession, fills a long-felt gap. From the author's preface we learn that this book "is planned to fulfill [the] great need for a relatively nontechnical yet academic approach to all phases of the subject. It is not and could not possibly be a thorough coverage of the whole field . . . but it does give a quick survey of general principles relating to nearly all aspects of the subject. The text is organized in twelve main chapters, roughly designed to fit a twelve-weeks' term, with four supplementary chapters (Part II) for schools offering a more comprehensive course on a semester basis. The treatment throughout is somewhat elementary, intended primarily for students with a year or less of college biology. . . ."

The 12 chapters referred to include such topics as the history of bird study, the bird compared to other animals, external and internal morphology, the annual cycle of reproductive activities, migration, distribution, food habits, and conservation. Part II discusses classification, fossils and evolution, bird study methods, ornithological organizations, and their journals. After each major topic there is a short selected list of references; there is an additional bibliography of 314 titles at the end of the book. These together permit the student to have at hand a quick source of references for additional study. There are 180 illustrations, from graphs to scenic vistas, including, of course, pictures of many different kinds of birds. Among the latter are photographs of stuffed specimens that somehow cause me considerable esthetic pain. I would be remiss if I did not point out that a few errors or lapses were noted, but these were not so numerous or so grave as to mar the general context.

As a whole the author has fulfilled his announced purpose. I find myself sympathetic with the choice of material (with the exception of that on feeding stations and bird-boxes) and with the method of presentation. Opinions will differ as to the position of ornithology as a college science course. If it is considered as a service course for teachers, naturalists, and others with a passing interest in birds, then this book will suit admirably. On the other hand, if ornithology is to be considered a zoological science requiring prerequisites similar to those required for other advanced

fields in zoology, then perhaps this book is too elementary. My first classroom experience with the book revealed that it was rather weak in respect to morphology and physiology, but I was able to supplement it readily with more detailed information whenever I thought that was needed. Otherwise the textbook served very well for my introductory course. Although there is no other book to compare it with, it is my feeling that Wallace's *Introduction to Ornithology* can stand on its own and will prove to be a boon to all teachers of ornithology.

HENRI C. SEIBERT

ZOO-SAFARI. *Bericht der Deutschen Zoologischen Ostafrika-Expedition 1951/52 (Gruppe Stuttgart).*

By Erwin Lindner. E. Schweizerbart'sche Verlagsbuchhandlung (Erwin Nägele), Stuttgart. DM 15.40. xii + 139 pp. + 2 pl. + 1 folded map; text ill. 1954.

From November 1951 to June 1952, the German Zoological East-Africa Expedition (5 scientists) traveled through Tanganyika and Kenya, collecting specimens and photographs. Particular emphasis was placed upon the insects (by entomologist Lindner, who led the group), birds, and larger mammals. In this pleasant little book, an informal log of the expedition is amplified for the general reader. A list of mammals is given, with indication of the provinces in which specimens were collected. In place of an index, there is an alphabetized list of the plants and animals referred to, arranged entirely by their scientific names. The sentences are straightforward enough to be read without undue effort by any graduate student with a knowledge of scientific German.

LORUS J. & MARGERY MILNE

FAUNAL AND ARCHEOLOGICAL RESEARCHES IN YUCATAN CAVES. *Bull. No. 33.*

By Robert T. Hatt, Harvey I. Fisher, Dave A. Langebartel, and George W. Brainerd. Cranbrook Institute of Science, Bloomfield Hills. $1.00 (paper). iv + 119 pp. + 12 pl.; text ill. 1953.

Yucatan is underlaid with fairly recent limestone and chalk deposits. Its climate alternates between six months of wet weather, followed by six months of dryness. There is little if any surface drainage, and the terrain is pocketed with caves formed by downfalling from the roofs of underground dissolution chambers. There is little soil in the area, and consequently the cave deposits are not of great depth. The caves reported on in this study lie along the Serrania, a low range of hills in the southwestern part of Yucatan province. In all, reports are made on 14 caves.

The mammalian, avian, amphibian, and most of the reptilian fauna of the caves was found to vary only slightly from the known recent fauna of the region, although some species represented in the cave material are now rare or extirpated in the surrounding area. Two new genera and species of iguanid lizards were recovered from the oldest deposits of one cave, regarded as being early post-Pleistocene in age.

No human artifacts of preceramic age were found. The earliest finds are dated as approximately 300 B. C. Human occupation of the caves seems to have been correlated with a dependable water supply.

This volume reports on the results of the 1929 and 1947 expeditions of Robert Hatt and summarizes the work of others, principally that of Mercer, who excavated in 1895. The Mercer bone collections have become lost, but his archeological collections still exist.

BRYAN P. GLASS

MAMMALS. *A Guide to Familiar American Species. A Golden Nature Guide. Sponsored by The Wildlife Management Institute.*

By Herbert S. Zim and Donald F. Hoffmeister; illustrated by James Gordon Irving. Simon & Schuster, New York. $1.95 (cloth); $1.00 (paper). 160 pp.; ill. 1955.

The abundance of unusually excellent colored plates will alone make this book a welcome addition to the bookshelf of the nature lover. Most of the larger animals are treated at the species level, but many rodents, bats, and shrews are not discussed below the level of the genus.

The text is necessarily brief, and while usually accurate, is inadequate to give more than a suggestion of mammalian biology. The inclusion of distribution maps supplements this to some degree. However, using this book alone one might be led to believe that there is but one species of *Myotis*, that *Tadarida* is not found in the southeastern United States, that pumas and mountain goats are verging on extinction while grizzly bears are not, or that the mule deer is a creature of the coastal forests while the black-tail is widespread over the region from the Rocky Mountains westward.

In this book as in other recent handbooks a real attempt has been made to standardize common names for mammals. It is to be hoped that success in this area of mammalogy may soon compare with the condition already attained in the field of ornithology.

BRYAN P. GLASS

LIST OF NORTH AMERICAN RECENT MAMMALS. *U. S. nat. Mus., Bull. 205.*

By Gerrit S. Miller, Jr. and Remington Kellogg. Smithsonian Institution, Washington. $3.50 (paper). xii + 954 pp. 1955.

For many years mammalogists have been awaiting the appearance of a checklist to succeed the one published by Miller in 1924. At last it is here and becomes the reference authority on nomenclatural matters.

It should be remembered that the critical date for this publication is January 1, 1953. No papers published subsequent to that date were considered. It is therefore, in a sense, already obsolete at the time of publication—an unfortunate fate common to all checklists.

In contrast to the latest checklist of Reptiles and Amphibians, the authors have made no attempt to inject personal opinion into their arrangements. The forms are listed exactly as they were in the literature, and reflect only the opinions of the latest revisers. For all active mammalogists this volume will be an indispensable working tool of the profession. It is to be hoped that the next revision will not be so long in making its appearance.

BRYAN P. GLASS

ANIMAL GROWTH AND DEVELOPMENT

CONTRIBUTIONS TO EMBRYOLOGY. *Volume XXXV, Nos. 231 to 241. Carnegie Inst. Wash. Pub. 603. Carnegie Institution of Washington.* $13.00 (cloth); $12.00 (paper). ii + 238 pp. + 83 pl.; text ill. 1954.

This volume of *Contributions to Embryology* contains 11 papers, 5 of which deal with some phase of development of man, 3 with the monkey, and one each with the baboon, lamb, and chick.

Within the past 14 years much information concerning the early development of man has been acquired from rare and valuable specimens recovered and made available for study through the concerted efforts of Arthur T. Hertig, John Rock, and their associates. The 36 specimens obtained by them so far range in developmental age from a segmenting ovum of 2 cells up to an implanted 14-day embryo. In the present communication, Hertig, Rock, Adams, and Mulligan describe the youngest of the stages collected, i.e., those prior to implantation, ranging from the second to the fifth day of development. Of the 8 specimens described, 4 are considered to be normal; 4 are definitely abnormal. The 4 normal specimens include a 2-celled stage, a morula of 12 cells, a blastula of 58 cells, and a blastula of 107 cells. On the basis of the clinical data recorded, the ages are estimated to be 36, 72, 96, and 107 hours, respectively. Despite the limited number of cases, it would appear that in man the blastocyst is prepared for implantation slightly more rapidly than that of the macaque monkey—the only other primate that has been adequately studied. Abnormal morulae are said to be relatively common in the human uterus.

In a close series of perfectly preserved embryos (stages X to XIV of Streeter's Developmental Horizons), George W. Bartelmez has studied with his usual care and insight the formation of neural crest from the primary optic vesicle in man. Although it has been long known that the optic vesicle becomes enveloped in a sheath of loose cells (mesenchyme) that separate it from the ectoderm, the origin of these cells from the neural crest has not been previously established. Bartelmez's findings show very clearly that the neural crest arises from the wall of the optic vesicle in the same manner as from other sites, e.g., the neural tube. While the fate of the cells of the optic crest cannot be determined from sectioned material, it is highly probable that in man the sheath cells, like those of some other vertebrates in which they have been analyzed experimentally, give rise to the pigment cells of the uveal tunic.

The third paper dealing with the development of man is one by L. J. Wells, entitled The Development of the Human Diaphragm and Pleural Sacs. It is true, as the author points out, that many of the obscurities that have been associated with the morphogenesis of the diaphragm and pleural sacs tend to disappear when their anatomical relationships are viewed in three dimensions in a closely graded series of embryos, such as that available for study at the Carnegie Laboratory. The primitive diaphragm is regarded by the author as a single structure with 6 blended regional subdivisions and 5 hiatuses, two of which, namely, the pleuroperitoneal canals, are temporary. The closure of the pleuroperitoneal canals is considered to be brought about by the growth of subjacent organs. It is quite probable that a part of the diaphragmatic muscle arises in situ from mesenchyme.

A comprehensive study of the development of the kidney has been carried out by Theodore W. Torrey. Again the abundant and excellent material available in the Carnegie collection has been used to great advantage towards clarifying and correcting some of the older concepts that have been handed down in textbooks for years without qualification or question. The concept of the pronephros, for instance, is found to have no reality in the embryo of man. The author furnishes for teaching a useful diagram which summarizes the principal steps in the early development of the human nephros.

The fifth and last of the papers concerned with man is contributed by Anna W. Chako and S. R. M. Reynolds, and is entitled Architecture of Distended and Non-Distended Human Umbilical Cord Tissues with Special Reference to the Arteries and Veins. In this study, use has been made of the third dimension in ascertaining the peculiar and unique arrangement of tissue components along the length of the cord. Among the topics discussed are the mechanism of vasoconstriction and the source of the abundance of Wharton's jelly in the constricted cord.

Of the 3 papers on the monkey, one by George W. Corner and George W. Bartelmez deals with 9 early abnormal embryos of the Carnegie macaque collection. In approximately half of the cases described the corpus luteum and the endometrium were found to be histologically normal. The abnormality of the embryo in these cases is thought to have resulted from constitutional defects of the zygote. In the remaining cases the possibility exists that the abnormality resulted from primary failure of the corpus luteum. It is interesting to note that in the monkey, as in man, the mortality rate is high in early developmental stages.

By introducing testosterone propionate into the maternal circulation of macaques during pregnancy, L. J. Wells and G. van Wagenen were able to induce female pseudohermaphroditism. The induced modifications, confined chiefly to the reproductive tract, persisted in some cases for several years after birth. No major changes occurred in the gonads, even in those cases in which it was assumed that injections were begun prior to their morphological differentiation.

The third and last paper concerned with the monkey is one by Elizabeth Ramsey. It is devoted to a study of the venous drainage of the placenta at various stages of gestation. Since the general vascularization of the placenta of the monkey has been previously worked out by her, particular attention is given in the present investigation to the morphology of the marginal sinus and the role it plays in the placental circulation.

In recent years a collaborative program has been arranged between the Carnegie Laboratory of Embryology and the Department of Anatomy of the University of the Witwatersrand for collecting and studying embryos of the baboon, particularly embryos in the early critical stages of development. Four of the 6 embryos obtained so far are described in the present communication by Christine Gilbert and Chester H. Heuser. Two of the embryos represent presomite stages, 12 and 20 days of age; two represent late somite stages, 30 and 34 days of age. The detailed study of these specimens has yielded important information relating to the timing of developmental events. Although the embryo of the baboon displays certain characteristic morphological features that are different from those of the macaque and man at comparable stages, there is a fundamental similarity in the sequence and in the timing of developmental phenomena in all three of these primates. The importance of investigating the embryos of other primates in order to elucidate problems in the embryology of man is, of course, well recognized.

A report of studies on the time required for the circulation of blood through the major portions of the vascular system of fetal and 2-day-old lambs is reported by S. R. M. Reynolds, G. M. Ardran, and M. M. L. Prichard. Data were obtained from cineangiographic recordings. It has been shown that after ventilation of the lungs, the circulation through the pulmonary vessels is more rapid, and the volume of flow increases approximately fourfold. A tabulated summary of the extensive data accompanies the text.

The final paper to be mentioned is a study in vitro on the localization of the erythrocyte-forming areas in the early chick blastoderm, by George W. Settle. The results are of considerable interest in showing not only the location and configuration of the hemopoietic areas of prestreak, primitive streak, and early somite blastoderms, but also in confirming the present-day concepts of cell movements in the early chick embryo.

All of the 11 papers are exceptionally well illustrated.

MARY E. RAWLES

ANIMAL MORPHOLOGY

AN INTRODUCTION TO FUNCTIONAL HISTOLOGY. *By Geoffrey H. Bourne. Little, Brown and Company, Boston.* $5.00. viii + 198 pp.; ill. 1953.

This little book presents a novel approach to histology. Functional interpretations are stressed, but there is no claim to completeness. The author's Preface points out the unevenness of information derived from the chief sources, such as histochemistry, electron microscopy, and the effects of endocrines and vitamin deficiencies. Hence the presentation differs for each subject, and considerable variety is offered. For example, in considering the liver, the conventional structural pattern is compared to the highly controversial views of Elias. Whatever the true histology of liver may be, a comparison of these two concepts stimulates the reader to make a critical evaluation of both. New viewpoints regarding structure and function develop, viewpoints that certainly would never have arisen had the conventional structural pattern alone been presented.

An unusually interesting chapter on technique deals with some of the more recent methods. The techniques of general histochemistry, enzymology (with data on buffers), vitamin demonstration, and autoradiography are succinctly presented.

The illustrations are most interesting throughout the book. Here the unusual subject material shows to best advantage. There are some excellent micrographs from the phase contrast, electron, and fluorescence microscopes, in addition to numerous ones of histochemical preparations made with the ordinary white-light microscope. These are supplemented by a few well-chosen drawings.

The text reads easily and the format is satisfactory, although more copious reference to sources would have helped. This unusual volume is called to the attention of histologists, in whose library it should find an acceptable place.

F. N. LOW

DIE MULTIPOTENZ DES MESOTHELS (*Metamorphose und Mimese der Zelle*). *Veröffentlichungen aus der morphologischen Pathologie, Heft 58. 13. Band (Heft 2).*

By Wolfgang Brandenburg. Gustav Fischer Verlag, Jena. DM 6.00 (paper). viii + 56 pp.; ill. 1953.

Brandenburg has examined the serous exudates in a variety of diseases and has found that mesothelial cells assume extremely diverse forms and even simulate tumor cells. He therefore concludes that the examination of the cells in such exudates cannot be used as a diagnostic test for the presence of cancer.

WILLIAM BLOOM

CONNECTIVE TISSUE IN HEALTH AND DISEASE.

Edited by G. Asboe-Hansen. Ejnar Munksgaard, Copenhagen. Dan. kr. 50.– 322 pp. + 1 pl.; text ill. 1954.

In an extremely lucid manner and in a compact form, the editor of this volume and contributors to it have presented a great mass of information about the many-sided problems involving connective tissue. Succinct summaries of the important work in a particular field are found throughout the 22 chapters. Of great help to the investigator interested in connective tissue, and to those only obliquely concerned with this field, is the excellent list of references after each chapter. The breadth in content of this volume is shown by the following chapter titles: Normal Morphology and Morphogenesis of Connective Tissue (Robb-Smith); On the Sulphate Exchange of Sulpho-Mucopolysaccharides (Boström); Hormonal Influence on Connective Tissue (Iversen); Connective Tissues and Cancer (Simpson); Arthritis (Ragan); and Some Systemic Connective Tissue Disorders Pertaining to Dermatology (Asboe-Hansen).

In an Introduction, the editor remarks: "After ages of relative inconspicuousness the connective tissue has been attracting increasing attention during the past 25 years, an attention that in the last decade has approached enthusiasm." Such enthusiasm, in my own opinion, should well be felt by a peruser of this volume.

JOHN A. ARCADI

THE NEUROANATOMICAL BASIS FOR CLINICAL NEUROLOGY.

By Talmage L. Peele. McGraw-Hill Book Company, New York, Toronto, and London. $12.50. x + 564 pp.; ill. 1954.

Although the title of this book suggests a special treatment of its subject, as if it were planned to correlate neuroanatomy with clinical neurology, it is primarily a new textbook of neuroanatomy. Emphasis is placed upon clinical applications rather than upon pure morphology, but not to a degree that differs from the current trend. There is, however, very little attempt to create a comprehensive structural picture of the nervous system before functional patterns are introduced. The inclusion of physiological interpretations and clinical findings along with basic anatomy is not favored by all teachers of the subject. It is my own conviction that a purely structural approach at the outset of the course yields the best eventual results. Once a structural concept of the nervous system has been established, students respond with satisfying alacrity to the teaching of functional systems, the malfunctions of which are readily interpreted in terms of previously acquired anatomical knowledge. When physiological interpretations are incorporated with the initial teaching of basic structure the students are stimulated, to be sure, but the trend of interest is directed toward uncontrolled speculation rather than fact-finding. Too much encouragement along such lines inhibits the acquirement of a reliable factual background because such acquirement is not only difficult, but by now, relatively dull. Students lacking such a factual background find it difficult to interpret cases in which physiological malfunctions present unusual patterns. Yet the question of proper technique in the pedagogy of neuroanatomy is a moot one, and many teachers favor the method used by the present volume.

It is evident that considerable scholarly effort and careful work have gone into the preparation of this book. The text, of course, is entirely new, and a goodly number of the illustrations are original. The organization of the text into 23 chapters is unique but largely conventional. The index is adequate for the specific structural and functional entities listed but is less satisfactory for broader topics, such as pathways for functional systems. Indeed, a more concise summarization of the anatomy and practical aspects of the important functional systems than can be found anywhere in the book would have helped. Throughout the text reference is made (by number) to the bibliography of 870 items which follows the last chapter.

This new textbook of neuroanatomy has been carefully planned and executed, but it has no features that distinguish it from other texts in its field. It should certainly be satisfactory to those to whom its approach happens to appeal.

F. N. LOW

ANIMAL PHYSIOLOGY

PERSPECTIVES IN PHYSIOLOGY. *An International Symposium, 1953.*

Edited by Ilza Veith. American Physiological Society, Washington. $3.00. xii + 172 pp.; ill. 1954.

This is an excellent collection of short essays written by a number of internationally known physiologists,

some of whom are quite philosophical about the situation this science finds itself in today. The theme is principally concerned with the present status of physiology in the various regions of the world, how it got to where it is, and who contributed to its development.

In Russia, according to Bykov, the science has been developing along the lines set out by Pavlov, and is based on the notion that in physiological studies the organism ought to be considered as a well-integrated unit, not as a machine. Bykov states that until the present century, physiology was guided by Western thinking, which is the approach to problems from the analytic method, that is, the study of phenomena by acute experiments. Russia's physiology appears to be based solely on "synthetical thinking," which makes use of chronic experiments.

In Mexico (according to Rosenblueth) and Argentina (according to Houssay), science is not in a very happy state. Generally speaking, university and government authorities in Latin America are not aware yet of the role of the basic sciences. There is a prevailing attitude common to most countries in the southern hemisphere that the function of the university professor is no different from that of an elementary grade school teacher. He should dogmatically present material in lecture form and periodically test the memory with standard examinations. That he should have a quest for knowledge, a scientific spirit, and the ability and desire to do research are not considered important qualities for his appointment. Students are indoctrinated with an excessive respect for the contents of books and the professor's word. University professors in most such institutions, particularly in the medical schools, are part-time employees with loyalties divided among many jobs that contribute to their living. There are, of course, some notable exceptions and, in one or two areas, great strides have been made in developing institutes of higher learning.

England, of course, has its problems in procuring animals for research, as in most sections of the United Kingdom there are active antivivisection societies; but R. A. Peters reports that this situation is steadily improving. Denmark, according to Lundsgaard, has little difficulty in obtaining animals for biological research, but has more serious difficulties in staffing, with competent men, its physiological laboratories. This is because the salaries at all stages of a hospital career are higher than the corresponding stages of a laboratory career. Thus, if a man starts a career in the laboratory and doesn't reach the top post, for any number of reasons, he is going to remain at a considerably inferior financial status than his colleagues who went into the hospital. The situation in Italy, in this respect, is also very bad. Stella reports that the very few opportunities there make the career of a physiologist not a very encouraging one, and many excellent men are forced to abandon physiology after serving several years of training as an assistant. Liljestrand writes on the situation in Sweden. Many American academicians will undoubtedly view with alarm the situation in that country. Frankly, it is amazing that any country should be so far behind the times! Do you know, for instance, that professors are appointed for life by the government after a free and open competition in which every Swedish citizen is eligible? Also, that no consideration whatsoever is given to the political or religious attitudes of the applicant. Furthermore, imagine any sane nation allowing a professor freedom to express himself on any question that he may be interested in! And in Sweden he usually does! Worse yet—he can openly criticize his superiors and authorities and not jeopardize his position or board and room. But, what is a thousand times more dangerous—*these same rights and prerogatives are extended to even such an individual as an associate professor!* As a full professor, I view with particular concern and alarm the latter situation.

The many customers of Homer W. Smith's offerings are well aware of the fact that he doesn't like Plato, a distaste I share. I would suggest that the purchaser of this book leave for dessert Smith's essay, The Philosophic Limitations of Physiology. It is a delightful literary treat.

DAVID B. TYLER

LABORATORY EXPERIMENTS IN PHYSIOLOGY. *Fifth Edition.*

By W. D. Zoethout. The C. V. Mosby Company, St. Louis. $3.50. 260 pp.; ill. 1954.

The revisions in this edition are mainly concerned with the sections and experiments dealing with the circulation, blood, muscles, and nerves. Those using this manual for their courses will have ample, well-described experiments from which to select those most suited for their facilities.

DAVID B. TYLER

MANUAL FOR LABORATORY WORK IN MAMMALIAN PHYSIOLOGY. *Revised Edition.*

By Fred E. D'Amour and Frank R. Blood. The University of Chicago Press, Chicago. $4.00 (paper). viii pp. + 60 experiments + iv pp.; ill. 1954.

This is a laboratory manual designed to provide a basis for a course in mammalian physiology in colleges and universities where practical considerations preclude the use of dogs or cats as subjects. Rats are used in some 60 experiments which cover most of the topics that would be required in a year's course. The major divisions and some of the experiments described are as follows: blood (blood volume and freezing point depression of plasma); heart and circulation (circulation time, cardiac output, renal hypertension); respiration;

digestion and metabolism (alloxan diabetes); excretion; endocrine system (adrenalectomy, hypophysectomy); nervous system (labyrinthectomy, conditioned reflexes); and antibody formation (anaphylactic shock). The procedures are carefully described and profusely illustrated. This manual should be of interest not only to physiologists but also to those whose work requires the use of rats as subjects.

F. P. CHINARD

PRÉCIS DE PHYSIOLOGIE. *Second Edition.*

By L. C. Soula. Masson & Cie., Paris. 3,500 fr. (cloth); 2,900 fr. (paper). vi + 1100 pp.; ill. 1953.

This is a concise, didactic summary of some of the essential facts of physiology, apparently as presented to medical students in France. The organization is unusual in that there are two major sections: the first on matters dealing quite broadly with nutrition, the second on muscle and nerve function. In the first section the following topics are covered: the utilization of oxygen and carbon dioxide production, energy and nutritional requirements including vitamins; digestion and absorption; the circulatory system; respiration; blood and the internal environment, renal function; intermediary metabolism; and the role of hormonal secretions in growth, bone formation, sexual function, and morphogenesis. In the second section are presented muscle function, the central nervous system, and the autonomic nervous system.

There are no references and few examples of data that would stimulate students to think for themselves. Controversial matters are not detailed. There are some errors of fact, and in some fields, particularly renal function, and acid-base and electrolyte relationships, the treatment is inadequate.

F. P. CHINARD

AVIAN PHYSIOLOGY.

By Paul D. Sturkie. Comstock Publishing Associates, a division of Cornell University Press, Ithaca. $6.00. xx + 423 pp.; ill. 1954.

This book is apparently the first one in any language to be devoted to the specialized physiology of birds. It deals mainly with the chicken, the duck, and the pigeon, since most research on bird physiology has been conducted on these species. It comprises a well balanced assemblage of studies on all the major organ systems, written primarily for students and research workers in poultry science and veterinary medicine. The book includes elementary discussions of physiological principles for beginners, combined, however, with the presentation of many data on birds which should be valuable to anyone interested in avian physiology. Two-fifths of the space is devoted to endocrinology and reproduction, a proportion reflecting the relatively greater research activity in these fields. Embryology is not included. Numerous references to original literature are placed at the end of each chapter. Interesting differences between avian and mammalian physiology are indicated. There are some lapses, e.g., the discussion of the eye does not mention iodopsin, the cone pigment which was isolated from the chicken retina in 1937. The discussion on respiration could have been better integrated. There is sometimes apparent the tendency, all too frequent in elementary texts, to string phenomena together by a thread of apparently rational explanation, regardless of the finer sensibilities of the specialist, as in the statement that "adrenalin . . . causes atrophy of the testes, probably in the same manner as desoxycorticosterone."

EVELYN HOWARD

LE MÉTABOLISME DU POTASSIUM ET SES PERTURBATIONS.

By H. C. Plattner. Masson & Cie., Paris. 1,000 fr. (paper). viii + 156 + iv pp.; ill. 1954.

The development of methods for the rapid estimation of sodium and potassium in biological fluids has led to increasing awareness on the part of clinicians of the importance of these ions in the body economy. The problems met clinically have played a significant role in stimulating directly or indirectly physiological and biochemical studies.

This is an excellent monograph on the clinical aspects of potassium "metabolism." There are three major sections. The first describes the more physiological aspects: relationship to water metabolism; the distribution of potassium in the several body compartments; the intake and excretion of potassium; sodium and potassium interrelationships; the pathogenesis of potassium disorders. The second section describes specific hyperkalemic disorders and their treatment; and the third section deals with hypokalemic disorders and their management.

The text is well written, and the bibliography is excellent but includes no references after mid-1952, so that no mention of aldosterone appears. Of particular value are the many case reports which detail examples of specific disorders and their management. While primarily of interest to clinicians, a monograph such as this may also be of value to those who teach physiological chemistry and to those whose investigations involve exchanges of ions.

F. P. CHINARD

LES RÉGULATIONS NEURO-VÉGÉTATIVES.

By Sandro Burgi; preface by J. Lhermitte. G. Doin & Cie., Paris. 680 fr. (paper). 175 pp. 1953.

For many years after neurophysiologists and neuropathologists had begun their intense investigation of problems of the functioning of the central nervous system, they neglected, to a great degree, the activity that has since been given many names, including the vegetative, visceral, or autonomic regulation. Even after this so-called—and perhaps badly so—vegetative system was recognized, it was studied within certain narrow limits. It is only in the most recent period that physiologists, psychologists, psychiatrists, and others have come to realize the nature and importance of this type of nervous activity and of the regions of the nervous system with which it is associated. Indeed, even today we are only on the threshold of a whole new area and conceptual framework embodying the role of autonomic activity in the integrated responses of the entire organism under normal and abnormal conditions. Recent developments have made it clear that the "autonomic" system is not "autonomic"; that it is not separate from the central nervous system, but that its varied activities are regulated by cell groups to be found at every level of the central nervous system, from the spinal cord up to and including the cerebral cortex; and, finally, that it is related to both conscious and unconscious factors which, in turn, are involved with the feed-back control systems responsible for normal homeostasis and any deviations therefrom.

Sandro Burgi has tried to present briefly certain aspects of this widespread regulating system. He discusses digestion, excretion, regulation of circulation, water balance, etc., and does not overlook the importance of the autonomic regulatory centers in the diencephalon and cortex. He is particularly interested in the fact that discussion of neurovegetative regulations perforce leads one into the sphere of the emotions. His understanding of some of the subtleties of such problems is clear throughout the work. In discussing the regulation of lipid metabolism, he states, for example, that "Nous nous demandons, cependant, si tous ces métabolismes et surtout ceux des albumines et des graisses, ne constituent pas des abstractions, fort utiles pour l'étude de la chimie physiologique, mais dont la réalité ne se retrouverait qu'au niveau de l'écorce cérébrale des biologistes. . . . Y a-t-il une régulation du métabolisme général, qui porterait soit sur la quantité, soit sur la qualité des échanges?" We run into such questions when considering certain aspects of homeostasis, for example.

It is good to see that the author realizes that autonomic activity is not all or none—or perhaps we should say on or off—but that the important question is often that of a modification of existing activity. His general framework is that which has resulted from a consideration of the works of Professor Hess (his teacher), and, for the most part, is very reasonable. It is too bad that so much recent work has been omitted. The major sins of the book, are, in fact, those of omission. Inclusion of recent studies of Hoff, Magoun, and others in America, as well as of a host of investigators in Germany, Switzerland, and France would have greatly increased the usefulness of the book. Perhaps an expansion of the concepts and bibliography will appear in a later edition.

R. G. GRENELL

DOCUMENTA OPHTHALMOLOGICA. *Advances in Ophthalmology, Vol. VII–VIII.*

Edited by G. von Bahr, J. ten Doesschate, H. Fisher-von Bünau, J. Francois, H. Goldmann, G. Lo Cascio, H. K. Muller, Jean Nordmann, A. J. Schaeffer, and Arnold Sorsby. W. Junk, The Hague. Guilders 125. 758 pp. + 24 pl. + 1 folded pl.; text ill. 1954.

The present issue of this important series contains the reports of two symposia: (1) an international colloquium on the circulation of the retina held at Strasbourg, France, June 15–16, 1951; and (2) a Netherlands symposium on strabismus.

The colloquium on retinal circulation deals most particularly with the method of ophthalmodynamometry devised by Baillart, an elder statesman of French ophthalmology. Ophthalmodynamometry is a procedure in which force is exerted to compress the eyeball, while at the same time the retinal blood vessels are observed with an ophthalmoscope. One can record the force required to produce a collapsing pulse or a cessation of flow in these vessels. If the force is applied in a standard fashion, conversion tables can be worked out that enable one to estimate the intraocular pressure corresponding to a given amount of compressing force. The pressure at which a collapsing pulsation appears in the retinal artery may be assumed roughly to equal the diastolic pressure in the ophthalmic artery. The pressure at which flow ceases in the retinal vessels may be assumed roughly to equal the systolic pressure in the ophthalmic artery. The physical, i.e., hydrodynamic, considerations involved in these estimates are discussed by Goldmann.

Using a given form of compressing applicator and a given conversion table, one can establish a linear relation between the ophthalmodynamometric estimate of blood pressure and that obtained by the usual sphygmometric apparatus with respect to the brachial artery (Bjork). This linear relationship is independent of local, i.e., retinal vascular, disease. If the conversion table of Baillart and Magitot is used, the regression line relating these two variables does not go through the origin, and the ratio of ophthalmodynamometric pressure estimate to brachial pressure estimate increases as the blood pressure increases. A substantial group of French ophthalmologists has habitually referred to observations in which the ophthalmodynamometric pressure estimate was greater than one-half the brachial pressure as "abnormal," and almost all of the instances of this "abnormal" ratio occur in cases of vascular

hypertension. Since the linear correlation relates to the degree of the vascular hypertension and does not differ significantly in various types of hypertensive vascular disease, the "abnormality" has, in itself, little diagnostic significance.

The bulk of the colloquium consists in the clinical analysis of ophthalmodynamometric and related measurements in a variety of disease states, and includes many shrewd and perspicacious observations on the nature of hypertensive vascular disease (Streiff, Couadau and Planques, Weigelin, Fritz, Francois, Baillart, et al.). Since these discussions, themselves, represent condensations and reviews, they cannot profitably be summarized in brief here.

The editors of this volume have adopted an unusual convention in respect to alphabetical abbreviations. I have myself for some time been annoyed by the tendency of American scientific publications to list the alphabetical abbreviation parenthetically at the first textual quotation. For instance, someone may mention the "run and see test" (RST) and thereafter refer to RST without further definition. The unwary reader who misses the first mention and is unable to comprehend the meaning of RST has to pursue his way backwards until he finds the first use of these letters in order to learn the definition.

In a recent issue of *Annual Reviews* this procedure has been elaborated by listing the first use of the abbreviation thus: RST[2]. It turns out that the elevated numeral is not an exponent but refers to a footnote back on the first page in which all the abbreviations that are to be used in this particular essay are enumerated and defined. This helpful complication is, of course, not to be confused with "RST (2)" in which the numeral refers to a reference in the bibliography.

In the present text all these complications are avoided by the simple expedient of leaving the abbreviations undefined. The reader who does not guess their meaning upon the first encounter will not be seduced into interrupting the course of his study by looking for an earlier footnote or definition, but can proceed forward in the expectation that new and intriguing puzzles lie ahead. Thus the most commonly used abbreviation in this text, P.A.R., turns out to mean "pression artérielle rétinienne" and to be identical with N.A.D., i.e., "Netzhautarteriendruck."

The symposium on strabismus was held on the occasion of the 107th meeting of the Netherlands Ophthalmological Society in December, 1943, and was continued in the 108th meeting in May, 1944. The symposium was printed and copies were distributed to the members of the society. Additional copies held for distribution to medical libraries and to interested individuals were lost during the German occupation. Republication of this symposium in English translation by *Documenta Ophthalmologica* is a most praiseworthy enterprise, for the scientific value of these contributions is extremely high, in spite of the severe stress of the war during which the original papers were prepared. The contributors to the symposium were van Heuven, van der Hoeve, Waardenburg, Weve, and Zeeman. In the final publication van Heuven's report is omitted, and an additional chapter is included by Fischer and Wagenaar on Binocular Vision and Fusion Movements.

The analysis of binocular vision, space perception, and the associated motor activities is a scholarly one and forms a solid basis for the more clinically oriented chapters that follow. Van der Hoeve, with his great facility for lucid exposition, lays bare the distinction between primary and secondary amblyopia in relation to squint. Waardenburg's chapter on Squint and Heredity includes the genetic analysis of much new material. Weve and Zeeman respectively report their experience in the surgical and non-surgical treatment of strabismus.

Of the contributors to this symposium, Fischer and van der Hoeve have since died. The current volume includes an obituary in memoriam of van der Hoeve, a distinguished and gracious person whose contributions to the science of ophthalmology have been eminent, and whose erudition and charm have been an important feature of international ophthalmological meetings for many years. Fischer, a refugee from Hitlerite Germany who was hidden and protected by his colleagues during the whole period of German occupation of the Netherlands, died in 1951 in the flowering of his scientific career.

The volume under review also contains an essay on Optokinetic Nystagmus, by Roelofs, and a report on Experimental Keratoplasty, by Yap-Kie-Tiong.

JONAS S. FRIEDENWALD

ANIMAL NUTRITION

VITAMINS AND HORMONES. *Advances in Research and Applications. Volume XII.*

Edited by Robert S. Harris, G. F. Marrian, and Kenneth V. Thimann. Academic Press, New York. $7.50. xii + 306 pp.; ill. 1954.

Another excellent compilation of review articles covering various aspects of the chemistry and metabolism of the vitamins and hormones has been presented in this volume. The authors are again to be congratulated for maintaining the standards of earlier volumes.

The chemistry of vitamin B_{12}, reviewed by K. Folkers and D. E. Wolf, is concerned with the structure of vitamin B_{12}, its various forms and their degradation products. The review does not cover the biological action of the vitamin. S. Kon and J. W. G. Porter discuss the intestinal synthesis of vitamins in the ruminant. Their article considers the preruminant calf, the establishment of the ruminant function, the adult ruminant, and other aspects of the problem. Two chapters are devoted to vitamin A. C. Nieman and H. J. K.

Obbink review the biochemistry and pathology of hypervitaminosis A and consider the interaction of excess vitamin A with thyroxine, calcium, and phosphorus, the vitamin B complex, ascorbic acid, vitamin D, and vitamin K. The vitamin A requirement of animal species is well covered in a paper by S. H. Rubins and E. DeRitter.

Other subjects reviewed in the current volume are: Disturbances in Nutrition relating to Liver Disease in Man (C. S. Davidson); Light Regulation of Hormone Secretion (J. Hammond, Jr.); Estrogens and Related Substances in Plants (R. B. Bradbury and D. E. White); and Effects of Estrogens on Domestic Fowl and Applications in the Poultry Industry (F. W. Lorenz).

R. Van Reen

Vitamin Manual.

Foreword by Norman Jolliffe. Published by The Upjohn Company, Kalamazoo. Free upon request (paper). 90 + vii pp.; ill. 1953.

This manual contains a concise description of each of the known fat-soluble and water-soluble vitamins. Each vitamin is discussed in respect to our present knowledge of its metabolic functions, clinical signs of deficiency, therapy, toxicity, and requirements. Major emphasis is placed on the role of the vitamin in human nutrition; however, numerous references to animal studies are also presented. Gross features of the deficiency syndromes are discussed and illustrated, along with the histological manifestations of each deficiency. In this convenient form, with profuse illustrations, this review should be of considerable value to practitioners, nurses, and students of nutrition.

R. Van Reen

Advances in Food Research. *Volume V.*

Edited by E. W. Mrak and G. F. Stewart. Academic Press, New York. $11.50. x + 538 pp.; ill. 1954.

As in previous volumes of this series, various subjects of primary importance to workers in the field of food technology and nutrition are reviewed in Volume 5 by leading authorities. B. M. Watts' discussion of oxidative rancidity and discoloration in meat concerns the oxidation of fats and the oxidation of heme pigments. Problems related to the use of sulfites and sulfur dioxide in the food industry are discussed in two papers by H. Gehman and E. M. Osman and by M. J. Joslyn and J. B. S. Braverman, respectively. An extensive treatment of statistical methods in food research is presented by B. Ostle and R. G. Tischer. This chapter should prove of great value and might well stimulate a more extensive use of statistical methods in food research. Other topics considered in this volume are: Flavonoid Compounds in Foods (E. C. Bate-Smith); The Color Problem in Foods (G. Mackinney and C. O. Chichester); and Composition of Wines (M. A. Amerine).

R. Van Reen

Feeding Poultry. *Second Edition.*

By Gustave F. Heuser. John Wiley & Sons, New York; Chapman & Hall, London. $7.50. viii + 632 pp.; ill. 1955.

It is pointed out by the author of this volume that more progress has been made in feeding poultry during the past 50 years than was made during the preceding 500 or even 1000 years. Since the advancement in our knowledge of nutrition has been rapid, this book will be of considerable value to feed dealers, poultry producers, and students in poultry husbandry. Approximately the first half of the text is devoted to general considerations of principles in feeding poultry, composition of plants, composition of rations, factors in making a poultry ration, and feeding systems and practices. In the last half of the volume, the author considers the more specialized topics of feeding young chickens, egg production, the management of breeders, and the feeding of other species of birds. The economics of feeding is a subject which must be considered by commercial producers and is presented in the final chapter of the book.

R. Van Reen

BIOPHYSICS AND GENERAL PHYSIOLOGY

Recent Developments in Cell Physiology. *Proceedings of the Seventh Symposium of the Colston Research Society held in the University of Bristol, March 29th–April 1st, 1954.*

Edited by J. A. Kitching. Academic Press, New York; Butterworths Scientific Publications, London. $6.50. x + 206 pp. + 1 pl.; text ill. 1954.

This interesting report contains the proceedings of the Seventh Colston Symposium held at the University of Bristol in the spring of 1954. The papers as a whole are excellent and give one a new outlook on the diverse fields in which research in cell physiology is currently taking place. First is a discussion of selective active transport by J. F. Danielli, who considers facilitated diffusion, the increased rate of permeation of substances such as sugars moving into tissues along a concentration gradient, and active transport for substances such as sodium and potassium which may move either with or against electrochemical gradients. Danielli suggests, from the analysis he presents, that his homogeneous lipid membrane is essentially a correct structural interpretation of the cell surface, but in this presentation he modifies that view to the extent of adding to the structure "polar pores" to explain the anomalous and rapid permeation of small molecules such as water and meth-

anol. In the second contribution to the symposium, H. J. Koch discusses the role of cholinesterase in the transport of sodium through the gills. The experimental results show that sodium transport is markedly depressed by substances which block the action of cholinesterase. The third paper, by Ussing, deals with membrane structure analysis as revealed by permeability studies. This considers principally the difference between the rate of transfer water penetrating without such a gradient. The conclusions essentially are that a pore type of membrane structure is indicated if the experimental results are to be properly explained. The next paper, by Keynes, is on the Ionic Permeability of Nerve Membranes, and is a summary of the observations on the transport of ions through nerve during rest and activity. E. W. Yemm discusses cellular oxidations and the synthesis of amino acids and amides in plants; and Hans Klenow, the biosynthesis of pentoses and their incorporation into mononucleotides.

There is a most interesting paper on desoxyribonucleic acid in gametes and embryos, by Hoff-Jørgensen; it shows the application of a very nice assay method for DNA. A paper by Brachet on The Nuclear Control of Enzymatic Activities points out that the nucleus is neither the center of cellular oxidations nor a storehouse or building place for all enzymes, and that it may be concerned mainly with the synthesis of nucleotides which control biochemical behavior. Waddington discusses the cell physiology for early development in a presentation that involves considering the hierarchy of synthetic processes that may be necessary to account for developmental phenomena. Regeneration in Planarians is discussed by Bronsted, and Synchronous Divisions in Protozoa by Zeuthen and Scherbaum, while Synchronism in Cell Division in Bacteria is discussed by Maaløe and Lark.

The symposium is concluded by papers on the Environmental and Genetic Control of Differentiation in Neurospora, by Westergaard and Hirsch, on The Control of Cell Division, by Swann, and on Suction in Suctoria, by Kitching.

Both in the diversity of subject matter and in the quality of the papers in the discussion, this report of the symposium impressed the reader most favorably. The volume should in addition be most useful to many individuals who are not specialists in these particular fields and who are trying to keep in touch with the very rapid developments now taking place.

L. J. MULLINS

ACTIVE TRANSPORT AND SECRETION. *Sympos. Soc. exp. Biol., No. VIII.*

Edited by R. Brown and J. F. Danielli. Published for the Company of Biologists on behalf of the Society for Experimental Biology; Academic Press, New York. $8.00. viii + 516 pp.; ill. 1954.

This symposium covers papers read at a meeting at Bangor (Wales) in July, 1953. The 27 papers, written by experts, provide an excellent review of the current state of the field of active transport in plant and animal tissues. The book is certainly indispensable reading for anyone working on the transport of substances across living membranes. The material presented is mainly from the experimental point of view, though several of the authors have gone into theory. There is an approximately even distribution between treatment of nonelectrolytes and electrolytes, and the experimental objects range all the way from subcellular units, such as mitochondria, through simple cells, such as yeast cells, red blood cells, or bacteria, to whole tissues or organs. Three of the articles deal with ion transport in nerve or muscle.

The reader will be struck by two things. First, there is yet to be found an adequate definition of the concept of active transport. The workers in the field are keenly aware of this, and several attempts are made in the book to arrive at one. It may not even be possible to arrive at a simple definition covering all cases, but it is encouraging that serious thought is being devoted to the problem. Second, it is increasingly clear that the lack of more definite information concerning the precise structure of living membranes poses a fundamental obstacle to real progress. There must be ways to examine physically the intimate architecture of these structures that are at once so thin, so delicate, and so complicated. One promising line of attack lies in the electron microscope studies of ultrathin sections, exemplified by the work of Sjöstrand and others. Another conceivable mode of attack would be the use of ultramicroscopic probes to measure electric gradients and other physical forces localized to distances comparable with membrane dimensions. However, until such information is at hand it seems that the price of progress in the field will continue to be a disproportionate amount of scientific effort to accomplishment.

PHILIP W. DAVIES

IONIZING RADIATION AND THE CELL. *Ann. N. Y. Acad. Sci., Vol. 59, Art. 4.*

Edited by Roy Waldo Miner; Leslie F. Nims, consulting editor; Leslie F. Nims (conference chairman), E. S. G. Barron, W. D. Bellamy, M. H. Bernstein, W. Bloom, R. S. Caldecott, F. J. de Serres, D. J. Fluke, H. Fricke, N. H. Giles, F. Hutchinson, B. P. Kaufmann, R. F. Kimball, E. J. Lawton, M. R. McDonald, C. W. H. Partridge, H. M. Patt, E. C. Pollard, E. L. Powers, R. Sellow, G. E. Stapleton, R. B. Uretz, and R. E. Zirkle. $4.00 (paper). Pp. 467–664; ill. 1955.

The present volume gives clear indication that the frequency of publications of symposia on radiobiological effects far outstrips the accumulation of significant data

and the formulation of new ideas. The result is largely a rehashing of old material, made somewhat more palatable by the addition of a fresh egg or two. Symposia, of course, are held for purposes of reappraisal and active exchange of ideas, but since the Oberlin volume was published in 1952 radiobiological appraisals have been far more numerous than the circumstances and status of the field deserve or warrant. The meager discussion following the presentations adds little to this volume. If justification of the present symposium is to be made, it lies perhaps in the fact that some tangible expression of the vast amounts of money being expended on radiobiological research is needed—a poor excuse, but a necessary one in these days of government-supported projects. This criticism indeed bites the hand that feeds, but at least let us be honest with ourselves.

The papers of the Yale group of biophysicists, and those by Caldecott, Giles et al., Kaufmann et al., Barron, Stapleton, and Patt need little comment, since the data to a large extent, and the ideas almost totally, have been presented in other journals before or since April, 1954, when this symposium was held. All, however, are up-to-date reviews ably handled, and therefore convenient to have in a single package. Zirkle's group considers in detail the effects of microbeams of protons and ultraviolet on chromosome movement and structure; Fricke presents a discussion and an extension of track effects in aqueous solutions; Bellamy and Lawson deal with the varying sensitivity of bacteria to energetic electrons; Powers and Kimball, separately, discuss radiation effects on *Paramecium*.

The papers present no single coherent attack on a subject, point of view or approach, but are as varied as the entire field of radiobiology. The volume, therefore, lacks synthesis and unity, and represents simply a group of reviews which, equally well, could have found a suitable place in so many separate and independent journals. It would seem that a moratorium on this type of "shotgun symposium" should be declared for some years to come.

C. P. Swanson

Sonics. *Techniques for the Use of Sound and Ultrasound in Engineering and Science.*

By Theodor F. Hueter and Richard H. Bolt. John Wiley & Sons, New York; Chapman & Hall, London. $10.00. xii + 456 pp.; ill. 1955.

Primarily, this is a treatment of the principles, possibilities, limitations, and techniques involved in production of sound, in its detection, and in its analysis. All is from the engineering point of view. Specific applications are overshadowed by considerations of the underlying physics. The biologist will feel the book to be incomplete, since it makes no mention of echo-location, sonar ranging, bats, or animal communication at frequencies audible to man and those above. But if he wishes to know the difference between piezoelectric and magnetostrictive transducers, or particle agglomeration, or acoustical relaxation mechanisms in fluids, the book describes the latest equipment and the mathematical relationships on which it has been designed.

Lorus J. & Margery Milne

BIOCHEMISTRY

Outlines of Enzyme Chemistry.

By J. B. Neilands, Paul K. Stumpf, and Roger Y. Stanier. John Wiley & Sons, New York; Chapman & Hall, London. $6.50. x + 316 pp.; ill. 1955.

Till this time there has not been available a book that offers a concise, general introduction to enzyme chemistry. In the present volume the authors have attempted to write such a book, and within the limitations imposed by some three hundred pages they have succeeded. The book should be especially valuable to the non-biochemist who is interested in information relating to the general properties of enzymes and the methods that are used to obtain such information.

Individual enzymes are not considered; instead information applicable to many enzymes is presented. The book is divided into four parts. The first concerns itself with the study of enzymes as chemical compounds. The second part deals with the application of physical-chemical principles to the description of enzyme-catalyzed reactions. The third section gives a classification of coenzymes and enzymes, with special attention to respiratory enzymes. Finally, in the last section enzymes are considered in their natural environment, the cell. This section stresses the idea of enzymes acting in sequence. A special chapter on the Synthesis of Enzymes, by Roger Y. Stanier, is also included.

In several of the chapters raw data from published research is used to work out some fundamental physical constant for a particular reaction. This should be of particular value to the person who is unfamiliar with the mechanics of using such data. Liberal references to specific research as well as to pertinent books and review articles are given at the end of each chapter.

Included in the book is some of the newer knowledge of enzymology, e.g., fatty acid oxidation, stereospecific hydrogen transfer, and protein synthesis. This has been done without ignoring earlier contributions. Unfortunately, the limitation of space has forced the authors merely to tabulate considerable information. Nevertheless a certain intimacy with the material is maintained by associating, whenever possible, the names of the investigators with a piece of work. Photographs of a number of these individuals are reproduced in the book.

Gale W. Rafter

FORTSCHRITTE DER CHEMIE ORGANISCHER NATURSTOFFE. *Tenth Volume.*

Edited by L. Zechmeister; authors, K. Alder, J. Asselineau, A. Chatterjee, L. Feinstein, M. Jacobson, E. Lederer, H. Mark, G. Rosenkranz, M. Schumacher, and F. Sondheimer. Springer Verlag, Vienna. $19.80 (cloth); $19.00 (paper). x + 530 pp.; ill. 1953.

The following topics are discussed in this volume: the diene synthesis, rubber chemistry, bacterial lipids, cortisone syntheses, Rauwolfia alkaloids, and insecticides of plants. The fundamental aspects of "rubberiness" are admirably treated by H. Mark. Asselineau and Lederer discuss first the unusual lipids found in bacteria, then the different types of bacteria, particularly the tubercle bacillus. Many biochemists will be surprised to learn that the bacterial lipids are free of sterols, almost free of glycerides, and that they contain numerous branched fatty acids. In view of the increased clinical use of *Rauwolfia* alkaloids, the article written by A. Chatterjee will be welcome to many readers. The volume is a worthy successor to the preceding volumes of this valuable series of progress reports.

F. HAUROWITZ

CAROTENOIDS. *Their Comparative Biochemistry.*

By T. W. Goodwin. Chemical Publishing Company, New York. $7.00. x + 356 pp.; ill. 1954.

This book fulfills a need for a compendium on the biochemical aspects of carotenoids, and will be a useful addition to any reference shelf. Although it may not properly be considered a textbook, the flowing style makes for relatively easy reading. A somewhat critical but necessarily brief discussion is interwoven through the voluminous reference citations. Many of the important problems of carotenoid biochemistry are sharply pinpointed against a sketch of existent knowledge.

A short introduction deals with the problems of definitions and nomenclature. Throughout the book, it is apparent that the author has made an attempt to bring some uniformity into the jumbled confusion of terminology appearing in the literature citations.

Part I, on Plant Carotenoids, includes physiological and biochemical aspects of carotenoid formation, function, and degradation. Discussions involving algae, fungi, and bacteria are included in this section.

Part II, on Animal Carotenoids, is somewhat more detailed with respect to the taxonomic classifications of the animals mentioned, and covers the gamut from marine invertebrates to mammals. Since less is known concerning the formation and function of these compounds in animals, the discussions are somewhat limited to descriptions. The function and reactions of vitamin A and its precursors are only briefly considered, since several more complete reviews may be found elsewhere.

A large amount of data and many spectra are included throughout the text. In addition, two appendices include a large collection of data on the carotene content of plants and their anatomical parts. The book is well indexed with respect to specific names, author, and subject.

R. D. DEMOSS

A SYMPOSIUM ON AMINO ACID METABOLISM, *sponsored by The McCollum-Pratt Institute of The Johns Hopkins University.*

Edited by William D. McElroy and H. Bentley Glass. The Johns Hopkins Press, Baltimore. $12.50. xvi + 1048 pp.; ill. 1955.

This volume contains the formal papers and discussions comprising a symposium held under the sponsorship of the McCollum-Pratt Institute in June, 1954. It is the fifth Symposium volume published under these auspices, and, like each of the preceding volumes, it provides an excellent survey of an important field of biochemistry. The *Symposium on Amino Acid Metabolism* begins with a relatively brief consideration of the general aspects of the subject: what might be called "type reactions" of amino acids in biological systems, including their incorporation into some naturally occurring peptides and adaptive enzymes. The major portion of the symposium is concerned with the biosynthesis and transformations of amino acids in unicellular and multicellular organisms, and many of the newly discovered interrelationships among the amino acids are discussed in detail. The final chapter—and by no means the least commendable contribution—is a penetrating summary of the entire proceedings, written by Bentley Glass.

As usual in these symposia volumes, many new experimental data are presented. Clearly, these will enhance the value of the book to the specialist working in this field. However, the fact that many of the papers also provide comprehensive reviews of the biochemistry of one or another amino acid makes this an invaluable reference book to specialist and non-specialist, alike.

SOFIA SIMMONDS

PROTEIN METABOLISM. *Methuen's Monographs on Biochemical subjects.*

By R. B. Fisher. John Wiley & Sons, New York; Methuen & Company, London. $2.50. x + 198 pp.; ill. 1954.

R. B. Fisher has performed a useful service in his critical reevaluation and presentation of the classical concepts of protein metabolism. Several important aspects of protein metabolism have been considered in the light of the available evidence, and many gaps in our knowledge have been pointed out. It is certainly healthy to reconsider periodically how present views came into being and what evidence is on hand in support of ac-

cepted notions. Clear but brief presentations have been made of such topics as protein digestion and absorption, nitrogen balance, fate of nitrogen (deamination, transamination, and urea synthesis), general aspects of amino acid metabolism, the turnover of nitrogen, nutritive value of proteins, and endocrine interactions in protein metabolism. Such topics as the special roles of certain amino acids in furnishing the nitrogen or carbon skeleton for the formation of porphyrins, purines, etc., have been omitted. This small monograph will be valuable in supplementing the unavoidable tendency of elementary textbooks to emphasize the known and well-established information. The advanced student who has digested the main facts of protein metabolism will derive much from the deliberately polemical viewpoint of this brief monograph.

EMIL L. SMITH

THE STRUCTURAL CHEMISTRY OF PROTEINS.
By H. D. Springall. Academic Press, New York; Butterworths Scientific Publications, London. $6.80. x + 376 pp.; ill. 1954.

In the 19th century the proteins were investigated mainly by physiologists and histologists who were interested in the biological roles of these complex substances. Since the time of Emil Fischer the respectability of proteins as proper subjects for study by organic and physical chemists has grown very rapidly. In a sense Springall's book represents a culmination of the tendency to study these large molecules from a purely chemical viewpoint. The proteins have become respectable indeed! However, it is somewhat surprising to find that the biological activities of these molecules are hardly mentioned. The book gives an excellent account of structural studies of the proteins: peptide syntheses, amino acid analyses, determination of sequences, and the physical properties of fibrous and globular proteins. Especially valuable is the extensive, clear presentation of x-ray investigations of fibrous and crystalline proteins. The book is very well written and, for the most part, is up to date in the material presented. For use as a textbook it must be assumed that the student will have to acquire separately a knowledge of conjugated proteins and of the activities of proteins as catalysts, oxygen carriers, and hormones. An especially valuable feature is the inclusion of indices for "named" proteins and natural peptides, as well as for authors and subjects.

EMIL L. SMITH

ADVANCES IN PROTEIN CHEMISTRY. *Volume IX.*
Edited by M. L. Anson, Kenneth Bailey, and John T. Edsall. Academic Press, New York. $10.50. viii + 542 pp.; ill. 1954.

This series of reviews has continued to maintain a uniformly high standard over the years; in fact, it would be hard to find another series of such quality. The present volume continues in the same fine tradition. It contains 8 articles which range over the entire field of protein chemistry, from metabolism in the whole animal to physical interactions in solution, from fibrous proteins to amino acids. The titles and authors are as follows: Metabolism of Glycine, by H. R. V. Arnstein; The Digestion of Protein and Nitrogenous Compounds in Ruminants, by M. I. Chalmers and R. L. M. Synge; the Resolution of Racemic α-Amino acids, by J. P. Greenstein; Naturally Occurring Trypsin Inhibitors, by M. Laskowski and M. Laskowski, Jr.; The Formation, Composition, and Properties of the Keratins, by W. W. Ward and H. P. Lundgren; The Molecular Structure of Simple Substances Related to Proteins, by S. Mizushima; Protein-Protein Interactions, by D. F. Waugh; and Physicochemical and Biological Aspects of Proteins at Interfaces, by D. F Cheesman and J. T. Davies.

Most of the articles represent unique contributions which achieve a synthesis of data and concepts difficult to obtain elsewhere. All of the articles are indispensable for the protein chemist who is concerned with the entire field, and most of the articles will interest the general biochemist.

EMIL L. SMITH

GLUTATHIONE. *Proceedings of the Symposium held at Ridgefield, Connecticut, November, 1953.*
Editors: S. Colowick, A. Lazarow, E. Racker, D. R. Schwarz, E. Stadtman, and H. Waelsch. Academic Press, New York. $7.50. x + 341 pp.; ill. 1954.

The scientific literature concerning glutathione has assumed voluminous proportions since the original report by F. G. Hopkins in 1921 of the isolation of this tripeptide in crystalline form from yeast. Practically all aspects of the chemistry and biology of the compound were considered at a symposium, held in November 1953, by a group of scientists from the U. S. A., Canada, Australia, and Germany; and both their formal papers and the discussions thereof are presented in this volume. The book begins with a very fine description of the organic chemistry and the methods used for the detection and assay of glutathione, and also of mercaptans and organic disulfides in general. This is followed by an excellent and detailed discussion of the biochemistry of glutathione, including its enzymatic oxidation and reduction, biosynthesis, relation to peptide and protein metabolism, and coenzyme functions, as well as of the role of SH compounds in cell growth and division. The concluding section, perhaps the weakest portion of the book, deals with the physiological action of glutathione and its relation to clinical medicine. Such a comprehensive survey of the current information on glutathione should prove of interest to

all biologists. Obviously, it will be extremely useful to those who are intimately concerned with the biological function of the compound. The readers of this stimulating book, like its editors, will feel indebted to the National Science Foundation and the Office of Naval Research for their support of the symposium.

SOFIA SIMMONDS

ADVANCES IN CARBOHYDRATE CHEMISTRY. *Volume 9.* *Editor, Melville L. Wolfrom; assistant editor, R. Stuart Tipson; associate editor for the British Isles, E. L. Hirst. Academic Press, New York.* $10.50. xviii + 426 pp. + 1 pl.; text ill. 1954.

Volume 9 of this well-known series contains 9 articles that deal with various specific aspects of current interest in the field of carbohydrate chemistry. The book opens with a discussion entitled Some Implications in Carbohydrate Chemistry of Theories Relating to the Mechanisms of Replacement Reactions, by R. U. Lemieux. The author gathered information pertaining to a few types of replacement reactions, chiefly dealing with the *O*-acyl derivatives of sugars, glycosides, and glycosyl halides. These substances were chosen because of the central role they play in carbohydrate chemistry. Here an attempt is made to correlate both stability and reactivity with structure. In the chapter, Alkali-sensitive Glycosides, C. E. Ballou is concerned with glycosides which are unstable to alkalis. According to this author, the fact that many glycosides are readily decomposed by base as well as by acid indicates that these possess properties characteristic of esters rather than of acetals.

The 2-Hydroxylglycals, by Mary G. Blair, deals with the chemistry of that class of compounds. Although the 2-hydroxylglycals have not assumed a particularly important role in carbohydrate chemistry, compounds of this family serve as useful intermediates in the preparation of anhydroalditols and as reference compounds in the proof of structure of certain naturally occurring members of this class.

The article Methyl Ethers of Hexuronic Acids, by G. O. Aspinall, is restricted to a discussion of the methyl ethers of the naturally occurring D-glucuronic, D-galacturonic, and D-mannuronic acids, and their derivatives. The methyl ethers of uronic acids occur as residues in a large number of different polysaccharides, particularly in gums and mucilages, and are important in the study of the detailed chemical structures of these polysaccharides.

The Raffinose Family of Oligosaccharides, by D. French, is a review of the chemistry and enzymology of raffinose and of those saccharides which are related to raffinose by virtue of having one or more α-D-galactopyranosyl groups in their structures. Although the economic importance of these oligosaccharides is at present limited, they are available in very large quantities in various plants and may constitute a potential food supply in the future.

In the chapter on The Conjugates of D-Glucuronic Acid of Animal Origin, R. S. Teague points out that although the D-glucuronic acid component of the conjugate is closely related to D-glucose, it is unrelated to the normal path of carbohydrate metabolism. The study of the conjugates of glucuronic acid has been largely responsible for growth of the field of drug metabolism and of detoxication. Here the chemistry and the metabolism of this class of compounds is thoroughly discussed and written from the physiological point of view.

In their chapter on the Color and Turbidity of Sugar Products, R. W. Liggett and V. R. Deitz review the recent literature, particularly that pertaining to spectrophotometric data, the visual appearance of the product, and the chemical structure and properties of the sugar's colorant.

The review on Carboxylmethylcellulose, by J. V. Karabinos and Marjorie Hindert, deals with the practical and potential applications of this cellulose derivative. The production of carboxymethylcellulose increased from approximately 2 million pounds in 1947 to 17 million pounds in 1951, approximately two-thirds of the latter amount being consumed in the detergent field and the remainder being spread over a wide variety of uses, such as drilling muds, foods, textiles, paper, and paint.

The volume concludes with a review on Paper Chromatography of Carbohydrates and Related Compounds, by G. N. Kowkabany. The following points are considered in the application of filter-paper chromatography to carbohydrates and related compounds: theoretical considerations; general details of the method as applied to qualitative separation and identification; applicability of the method to different classes of carbohydrates and related substances; quantitative separation; modifications in technique; and limitations of the method.

The volume also contains an obituary of the late eminent carbohydrate chemist, C. S. Hudson, written by M. L. Wolfrom. Hudson was one of the founders of the *Advances of Carbohydrate Chemistry* and was its chief editor for several years preceding his death. Readers will miss his frequent contributions to the series, always notable by his logical and lucid style.

W. Z. HASSID

THE BIOCHEMISTRY OF SEMEN. *By T. Mann. John Wiley & Sons, New York; Methuen & Company, London.* $2.90. xiv + 240 pp. + 7 pl.; text ill. 1954.

In this, the most recent of the Methuen Monograph series, Mann has presented an excellent account of the current status of the biochemistry of semen. Much of it

compiled from the author's significant contributions during the past decade, and augmented by extensive considerations of the work of many other investigators, this critical review integrates a rich supply of basic information which has originated in the laboratories of biochemists, physiologists, cytologists, embryologists, and applied biologists.

The Biochemistry of Semen will certainly prove of great interest and usefulness to many whose specialities may be as diverse as cellular biology, reproductive physiology, urology, and animal husbandry. Broad in scope, thoughtfully presented, well organized, adequately indexed, and carefully documented with over a thousand selected references, this book will long stand as a handy and thoroughly readable reference work in this expanding field of investigation. No small token of gratitude is due the author for his time and thoroughness in bringing the material together. Appreciation is also due the British Agricultural Research Council for its long-range and broad-minded policy and support of the investigations by Mann and his colleagues.

The monograph is an expanded and up-to-date version of the author's reviews which appeared in 1949 and 1951. Its various chapters deal with the chemical, cytochemical, physiological, and metabolic characteristics of spermatozoa and seminal plasma. Predominantly concerned with mammalian semen, the book includes frequent references to comparable and contrasting conditions in other vertebrate and invertebrate groups. The biochemistry of human semen receives its just share of attention. Whenever plausible, the metabolic characteristics of semen, studied in vitro, are related to the matter of fertility. Cautious in generalizing from results obtained in work on one type of spermatozoa, Mann draws upon the biochemical variations in the gametes of different species to elucidate the wide variety of metabolic patterns shown by these cells.

Although it is not easy to single out a few for special emphasis from the many interesting discussions in such a well-packed volume, I personally found certain topics particularly noteworthy: the methods of extractions and analysis of sperm nucleoproteins and deoxyribonucleic acid, the production of fructose by the accessory glands and the subsequent fructolysis by sperm in vitro, the nature and significance of the lipid metabolism of spermatozoa, the attempts and final successes in preserving spermatozoa at subzero temperatures, and the background and chemistry of the semen-detection tests, the Barberio reaction, and the Florence test, which are used in forensic medicine.

Mann has, moreover, an easy way of drawing on the past, conversant as he is with the historical tradition which underlies many of the "recent advances" in this area of research. It is refreshing if not surprising to read of Leeuwenhoek's discoveries of spermine crystals, the studies of Vauquelin (1791) on the chemical composition of semen, the "deep-freeze" experiments by Spallanzani (1776) on spermatozoa temporarily immobilized in snow, the toxicity of heavy metals to sperm as investigated by de Quatrefages (1850, 1853), the beneficial effects of potassium ions on sperm motility as described by Newport (1853), and the descriptions by Koelliker (1856) of the effects of hypotonicity on these cells.

By virtue of the methods involved, the scope of *The Biochemistry of Semen* is almost entirely a record of analyses based on conditions in vitro. It is incumbent upon the readers of this monograph to follow up with investigations of sperm behavior in vivo. It is here that our knowledge is deficient. Mann points out, for example, that "the metabolism of epididymal spermatozoa which are often immotile, but capable of long survival, is as yet only poorly understood"; and again, "it remains for further study to ascertain what type of carbohydrate metabolism predominates in spermatozoa during their existence in either the male or female genital tract." Having this monograph at hand will certainly facilitate the investigation of such problems.

DAVID BISHOP

EXPOSÉS ANNUELS DE BIOCHIMIE MÉDICALE. *Quinzième Série.*

By P. Boulanger and J. Montreuil, P. Favarger, A. Gajdos, B. Glasson, D. E. Green and J. Nordmann, E. Havinga, H. A. Krebs, J. Maisin, G. Lambert and E. Van Duyse, J. Roskam, G. Schapira and J. C. Dreyfus, and F. G. Young. Masson & Cie., Paris. 2,120 fr. (paper). ii + 284 pp.; ill. 1953.

The subjects reviewed in this 15th volume are: growth hormone (Young); oxidative phosphorylation (Krebs); the cyclophorase system and mitochondria (Green and Nordmann); photosynthesis (Havinga); acetylases and esterases (Glasson); the structure of ribonucleic acids (Boulanger and Montreuil); experimental cancer and "somatic mutations" (Maisin, Lambert, and Van Duyse). Of more clinical import are reviews on salicylate therapy (Roskam), on cholesterol and atheromatosis (Favarger), and on iron metabolism (Schapira and Dreyfus).

These reviews, like those of earlier volumes, are authoritative, well written and liberally illustrated. The bibliographies have been improved. Fewer errors are evident in the citations, and most of the names of authors now appear to be spelled correctly.

F. P. CHINARD

METHODS OF BIOCHEMICAL ANALYSIS. *Volume I.*

Edited by David Glick. Interscience Publishers, New York. $9.50. x + 522 pp.; ill. 1954.

The task of keeping abreast of the many changes in biochemical technology is becoming increasingly difficult for the individual scientist. Not only are the

analytical methods scattered throughout a voluminous literature, but space limitations in the journals at times necessitate the omission of detailed descriptions of biochemical techniques. An up-to-date review series for analytical biochemical methods is therefore most welcome.

Methods of Biochemical Analysis, Volume I, is the first in such a series which is to include "methods of chemical, physical, microbial and (if necessary) animal assays—as well as basic techniques and instrumentation for the determination of enzymes, vitamins, hormones, lipids, carbohydrates, proteins and their products, minerals, antimetabolites, etc." Individual chapters are so organized as to contain "a discussion of the background and previous work, a critical evaluation of various approaches and a presentation of procedural details of methods recommended by the authors."

As might be expected from the list of distinguished contributors, the individual topics are covered with admirable authority and clarity. In addition, the methods and discussions of them are meticulously documented with references to the literature.

Subjects for Volume I have been chosen quite apparently for their timeliness. They include analytical techniques for SH groups, phenolic compounds, antibiotics, vitamin B_{12}, ascorbic acid and related compounds, adrenol steroids, sugar mixtures, I^{131} compounds from the thyroid gland, choline, nucleic acids, raffinose and kestose, ATP and related compounds, catalase and peroxidase, hyaluronidase, serum lipoproteins, and urinary neutral 17-ketosteroids. There is also a chapter on zone electrophoresis. As this list of diversified and primarily unrelated topics indicates, the scope of this new series is exceptionally ambitious. In its all-inclusiveness lies the weakness of Volume I taken *by itself*.

There are sections for the endocrinologist, the enzymologist, the radiochemist, and the biochemist in quest of vitamin or organic group assays. By necessity one volume can include only a small section for each, and thereby temporarily places itself at a disadvantage with new or revised well-coordinated texts, which are specialized within a more limited field.

In conjunction with the publication of additional volumes in this series, however, *Methods in Biochemical Analysis*, Vol. I, should attain the inherent usefulness, as a practical, overall and up-to-date reference, which the high quality of its individual chapters merits.

CLAUDE F. BAXTER

A MANUAL OF PAPER CHROMATOGRAPHY AND PAPER ELECTROPHORESIS.

By Richard J. Block, Emmett L. Durrum, and Gunter Zweig; with the cooperation of Raymond LeStrange, Winston H. Wingerd, and Kathryn W. Weiss. Academic Press, New York. $8.00. viii + 484 pp.; ill. 1955.

This may be considered a 2nd edition of *Paper Chromatography. A Laboratory Manual* by Block, LeStrange, and Zweig, 1952 (*Q.R.B.*, 28: 205. 1953), with a new section on paper electrophoresis by Durrum. In this rapidly expanding field it is not unlikely that manuals describing methodology in detail will be out of date at the time of publication. Since 1948 over 300 papers have appeared on paper electrophoresis alone, and the variations in procedure are almost as numerous as workers in the field. Modifications of modifications of modifications go on endlessly to suit local laboratory facilities and conditions, and most of us who have used any of these analytic tools have contributed our share to the variations in techniques. The purchaser of manuals such as these should be aware of this state of affairs, particularly so in zone electrophoresis.

Despite these considerations, this manual is a very desirable addition to our libraries. The part dealing with paper chromatographic techniques is fairly complete, with detailed descriptions for the quantitative analysis of amino acids, proteins, carbohydrates, aliphatic acids, steroids and bile acids, purines, pyrimidines, phenols, aromatic acids, porphyrins, antibiotics, vitamins, and a large number of miscellaneous organic substances. The part on paper electrophoresis is chiefly concerned with basic principles and methodology. Durrum organizes this part well and classifies the procedures for discussion into a few basic types: (1) the closed-strip techniques (evaporation prevented); (2) the semi-closed techniques (evaporation permitted); and (3) the open-strip method (evaporation permitted). Also included are two very short chapters dealing with two-dimensional techniques and continuous electrophoresis.

DAVID B. TYLER

MICROBIOLOGY

MUMPS, MEASLES & MOSAICS. *A Study of Animal and Plant Viruses.*

By Kenneth M. Smith and Roy Markham. Frederick A. Praeger, New York. $4.00. xii + 160 pp. + 17 pl.; text ill. 1954.

In the New Naturalist series, which is concerned with the natural history of Britain, this volume is the second to deal primarily with micro-organisms. The first of these, *Fleas, Flukes, and Cuckoos*, was concerned with the principles of parasitology as exemplified by the macroscopic and microscopic parasites of birds. The present book extends this general topic to the viruses, which may be regarded as parasites at the cellular level. It is pleasing to see discussions of disease-producing agents presented to the layman in the framework of natural history. General thinking about infectious disease still includes some elements of the medieval concept of disease as an unnatural visitation. Books like this will, we may hope, eventually lead to the correct orientation.

Mumps, Measles & Mosaics is an attempt to bring together the essential facts common to viruses whether their host happens to be man, his domestic animals or plants, or insects or bacteria. This endeavor to extract basic principles common to all viruses is commendable and largely successful. Its collapse in the chapter on methods of control probably means only that our methods are directed at a superficial level.

As would be expected from the backgrounds of the authors, most of the book is about plant viruses. Considerable information is given concerning those encountered in garden and farm, including their recognition, means of transmission and dispersal by insects and otherwise, and what their presence means economically. In the discussions of animal viruses, the authors are on less familiar ground and give comparatively scant information. Unfortunately, several errors have crept in, the most serious of which involves a confusion between active and passive immunization.

Noteworthy special topics are the relation of viruses to tumors, and the use of viruses for biologic "warfare" against insects. The final chapter describes some of the simpler basic techniques by which "any reader who has a glass house" can perform transmission experiments himself.

The illustrations are well done and include several electron micrographs. There is an index and a glossary which will be helpful to the uninitiated reader.

FRANCIS B. GORDON

HEALTH AND DISEASE

WONDERS OF MODERN MEDICINE.

By Steven M. Spencer; foreword by George F. Lull. McGraw-Hill Book Company, New York, Toronto, and London. $4.00. xxiv + 276 pp. 1953.

The tremendous strides which have been made in the field of medical science during the past decade have kept the busy physician literally "running" to keep abreast of current knowledge and practice. In many instances the man in the street has had only the faintest glimmering of what has been accomplished and what is in prospect relative to many of his ills and ailments. It is fortunate indeed that the job of informing the public of the progress in this important field of human endeavor is assigned to writers with such interest, knowledge, and ability as are exhibited by the author of the present volume. As science writer for the *Saturday Evening Post* he has earned the plaudits of the medical profession as well as the public for the clarity, authenticity, and comprehensiveness with which his presentations are made.

Most of the topics covered in this volume appeared originally in the *Saturday Evening Post* over the past ten years, and, with certain necessary revisions and additions, they have been brought up to date for inclusion in the present volume. Twenty topics are presented, ranging from The Heart Menders and The War on Cancer, to Medicines from the Soil, and The Gamma-Globulin Story. Written in an extremely interesting fashion in "down-to-earth" language, each story traces one of the wonders of modern medicine from its earliest beginnings, through its trial in the experimental and clinical laboratories, and on to its present place in the physicians' armamentarium for the cure or control of disease or disablement.

In the words of Dr. George F. Lull, Secretary and General Manager of the American Medical Association, in his Foreword, "The twenty chapters in this volume are not only informative and engrossing, they are also inspiring and heartening. For through each of them runs a strong thread of hope for even greater medical progress in the years ahead—progress which will still further alleviate human suffering, save lives, and improve the health of mankind." A detailed index is appended.

B. AUBREY SCHNEIDER

Meredith's HYGIENE. *A Textbook for College Students on Physical, Mental, and Social Health from Personal and Public Aspects. Fifth Edition.*

By Arthur F. Davis and Warren H. Southworth. The Blakiston Company, New York and Toronto. $6.00. xvi + 906 pp.; ill. 1954.

The fifth edition of this well-known and widely used textbook maintains the same high standards of excellence in both subject matter and presentation which have been exhibited in the earlier editions and which have been responsible for its popularity over the past thirty years. Following the basic philosophy and format of the earlier editions, the present authors have brought the volume up to date by reworking the text, adding, altering, and rearranging where necessary.

Following the introductory chapter on the health situation in the United States, the remaining 57 chapters are grouped into 8 major topics. The Body in Health and Disease; Forces for Health; The Problem of Infection; Some Major Health Problems; First Aid in Injury and Illness; The Hygiene of Everyday Life; Family Hygiene; and, Mental Health. Written in a most interesting fashion and profusely illustrated, the text is designed not only for the purpose of imparting information, but also for developing correct attitudes toward personal as well as community health.

A list of 16 mm. educational films (with sources) for use in conjunction with the presentation of the subjects under each of the 8 major topics of the text is provided in a 15-page supplement. A list of sources of materials for teachers of college hygiene, a lengthy bibliography, and a detailed index conclude the volume.

B. AUBREY SCHNEIDER

HEALTHIER LIVING. *A Text in Personal and Community Health. A Health Education Council Book. By Justus J. Schifferes; introduction by John E. Sawhill; illustrations by Louise Bush. John Wiley & Sons, New York; Chapman & Hall, London.* School Edition, $5.75; Trade Edition, $6.75. xxxii + 928 pp.; ill. 1954–55.

The ideal textbook for a college course in health education has probably never been written, but in terms of subject matter, interest, and method of presentation, the present volume is certainly a monumental step in the right direction. Written, as the author indicates, "to the prescription of 300 college physicians, educators and administrators," the book had its genesis in the Third National Conference on Health in Colleges, held in New York in May, 1947. Working with the official report of the conference, *A Health Program for Colleges*, which made specific recommendations as to the desirable content of a college course in personal and community health, the author has spent six years gleaning, selecting, preparing, and arranging the materials for this superb text.

Written on the premise that health represents a "core area" in education, and that it is basic to all social progress, the work draws from many disciplines, including history, literature, anthropology, sociology, psychology, and even the basic teachings of the world's prominent religions. Recognizing the fact that the basic physiological functions of the body are modified by the human mind and emotions, and that they occur in a social setting, the author has defined his method of presentation as a "multidisciplinary approach to sociopsychosomatic medicine."

Beginning with the personal and family phases of healthful living, and proceeding through the community, national, and world aspects of health as related to social development, the volume provides for the ever-widening interest of the college student. Following a brief orientation to the philosophy of healthier living, the text is divided into 4 approximately equal sections dealing with family living, mental health, personal health, and community health. The subject matter is developed with due regard for the interests of the students. For example, the structure and function of the respiratory and circulatory systems are presented against the background of necessity in athletics, and the intricacies of the endocrine system are woven into the discussions of the reproductive process.

The 53 chapters of the book are organized into 26 independent and self-contained teaching units, complete with references for further reading and questions for discussion and review. The 20-page index enhances the value of the work as a resource volume.

In the hands of a properly inspired teacher, this textbook should do much to dispel that basic ignorance of biological and scientific facts about healthful ways of living which has plagued so many "well educated" people in the past.

B. AUBREY SCHNEIDER

TEXTBOOK OF COLLEGE HYGIENE.

By Oliver E. Byrd. W. B. Saunders Company, Philadelphia and London. $4.50. xvi + 444 pp.; ill. 1953.

TEACHER'S MANUAL FOR USE WITH TEXTBOOK OF COLLEGE HYGIENE.

By Oliver E. Byrd. W. B. Saunders Company, Philadelphia and London. Paper. 44 pp. 1953.

A thorough exploration of the health interests and needs of college students prefaced the author's efforts in the preparation of this concise and well-organized text. From such exploration there emerged some thirty major health topics which have been covered in the discussions from the standpoint of both personal and community relationships. Beginning with such items of primary interest to the graduating college student as Health in Marriage, Pregnancy and Childbirth, and Infant and Child Care, the volume presents a wealth of information regarding mental health, nutrition, alcohol, drugs, tobacco, immunization, communicable and chronic diseases, and accidents. Throughout, emphasis is placed on the functional and public health approach to the subject rather than upon purely anatomical or physiological considerations. Each chapter is terminated with a list of review questions and a selected list of publications for further reading. The work is carefully indexed.

A brief manual with suggestions as to methods of presentation and procedures for insuring a high degree of class interest and participation is available from the publishers for use in conjunction with the text.

B. AUBREY SCHNEIDER

FLUORIDATION AS *A Public Health Measure. Edited by James H. Shaw. American Association for the Advancement of Science, Washington.* $4.50 (AAAS members $4.00). viii + 232 pp.; ill. 1954.

This monograph is the third in a series, published by the American Association for the Advancement of Science, concerned with the ingestion of fluorine as a dental health measure. The first of the series, entitled *Fluorine and Dental Health*, and published in 1941, comprised the proceedings of a symposium devoted to the subject at the December, 1940, meeting of the A.A.A.S. at Dallas, Texas. The second volume, entitled *Dental Caries and Fluorine*, was derived from a similar symposium held in Cleveland, Ohio, in 1944. The first volume dealt primarily with the description, etiology, and epidemiology of mottled enamel; the second, with

the beneficial aspects of the ingestion of optimal amounts of naturally occurring fluorine in water supplies during the period of tooth development.

The present volume, representing the proceedings of two symposia (held in 1951 and 1952), with the addition of four manuscripts, completes the series by presenting the evidence thus far accumulated on the effectiveness of supplementing naturally low-fluoride water supplies with optimal amounts of fluorine in an attempt to improve dental health. The 11 papers, dealing with that many aspects of the problem, have been prepared by authorities in their respective fields. Each chapter is well documented, the volume listing a total of some 460 references.

For the public health worker, the water supply engineer, the civic official or the interested layman, the data and discussions presented in this volume will provide the answers to many questions which may arise in any prospective fluoridation project. The information should adequately cover the objections of those who oppose fluoridation as a public health measure. The numerous charts, tables, and other illustrative materials contribute to a fuller understanding of the textual materials. There is a short index.

B. AUBREY SCHNEIDER

ORAL PATHOLOGY. *A Historical, Roentgenological, and Clinical Study of the Diseases of the Teeth, Jaws, and Mouth. Fourth Edition.*

By Kurt H. Thoma. The C. V. Mosby Company, St. Louis. $22.50. xviii + 1536 pp. + 34 pl.; text ill. 1954.

This "Bible of Oral Pathology" is again, as in previous editions, a master work. It is so complete and so profusely illustrated that it has outgrown textbook proportions and has become an encyclopedia. Everything belonging to the field is described and each section is supported by a full list of references. There are 92 colored plates, and the index is extensive. The author and the publishers would do a great service to undergraduate dental students by publishing an introductory textbook of not over 400 pages, selected and condensed from the present work.

JOHN A. CAMERON

ADVENTURES IN ARTIFICAL RESPIRATION.

By Peter V. Karpovich. Association Press, New York. $7.50. xvi + 303 pp.; ill. 1953.

This is an excellent book dealing with a special subject. It traces the evolution of artificial respiration from very primitive times through the pioneering studies of Hall, Silvester, Howard, Schafer, and Nielsen. It is complete in much detail and will serve as a standard reference on the subject for years to come. Over 100 different procedures are fully described, including the hazards to the body and lungs that are involved due to inexpert manipulation and other causes. Much of the tabular material and many illustrations are original and are chosen with care.

This book is particularly recommended for obstetricians and nurses and should be in the libraries of all medical schools and, of course, all first-aid stations.

DAVID B. TYLER

THE PHYSIOPATHOLOGY OF CANCER. *A treatise for investigators, physicians, and students.*

Edited by Freddy Homburger and William H. Fishman; 28 contributors; Foreword by C. C. Little. Paul B. Hoeber, Medical Department of Harper & Brothers, New York. $18.00. xviii + 1031 pp.; ill. 1953.

The editors have admirably brought together in one unabridged volume the pertinent present-day knowledge in each of the vigorous fields of cancer research. The 28 contributors, well versed in their particular subjects, have been objectively critical of each contribution to the overall research problem. The result is an informative working analysis of the progress that has been made.

The book has been divided into four parts: Biology; Chemistry and Physics; Clinical Investigation; and Practical Applications. This arrangement allows the reader to be led from the basic studies through the problem of clinical investigations to the practical applications of the results of basic research in the diagnosis and treatment of cancer.

The Physiopathology of Cancer can be read to advantage by the student investigator and the practicing physician. A copy should be available for reference and periodic review to any oncologist.

ROBERT G. CHAMBERS

PSYCHOLOGY AND ANIMAL BEHAVIOR

THE BEHAVIOUR AND SOCIAL LIFE OF HONEYBEES. *By C. R. Ribbands. Hale Publishing Company, Hopeville, Ga.; Bee Research Association, London.* $4.50. 318 pp. + 9 pl.; text ill. 1953.

In recent years a number of very fine books have appeared that deal with one or another aspect of the biology of bees, and Ribbands' book is assuredly among the best and most useful of them. It will interest not only students of insect behavior, of bees in particular, and of insect societies, but also the general insect physiologist as well. Indeed, the entire outlook and development of this book is founded in general and special physiology.

A preliminary section, The Roots of Behaviour (57 pp), deals with the physiology of the sense organs and the experimental analysis of their thresholds, ranges, and characteristics. Thereafter sections on Individual Behaviour in the Field (78 pp), and Communication Between Honeybees (44 pp), relate direct evidence and experiments that bear on a honeybee's rapport with its environment, with pollen sources, foraging, training to crops, recognition of sister bees, transfer of information, and so on. The final series of chapters, entitled Life within the Community (128 pp), is by all odds the most interesting section of all. It is too bad that Ribbands, when concluding, did not choose to discuss the social life in Hymenoptera generally, rather than of honeybees specifically. His overall conclusion is a familiar one, namely that the bee family has evolved as a unit, and as a society, by successive restrictive adaptations to a food supply, the large-scale collection and management of which represents a triumph of insect evolution.

Perhaps the most notable feature of this book, aside from its excellent coverage, is the manner in which it treats its subject. Stylistically it is almost telegraphic in its concise expression, yet little more could be asked. It is lucid, nearly always giving the reader a remarkably clean-cut summary of how the experiments cited were carried out, what the chief results were, and the degree to which conclusions may be drawn. Should the reader wish more information than an immediate passage provides, an excellent index, as well as a bibliography of some 600 titles, will point it out if it exists. Finally, the photographs and diagrams that illustrate the text are uniformly well chosen and well executed.

Concluding his prefatory comment, Ribbands remarks that "this book is a consequence of the work of Professor Karl v. Frisch, whose discoveries aroused my interest in honeybee behaviour." All in all, it is a fine and useful tribute to v. Frisch's beautiful and now universally known research on the behavior and biology of honeybees.

KENNETH W. COOPER

THE DANCING BEES. *An Account of the Life and Senses of the Honey Bee.*

By Karl von Frisch; translated by Dora Ilse. Harcourt, Brace & Company, New York. $4.00. xiv + 183 pp. + 30 pl.; text ill. 1955.

Five years after the publication of *Bees: their Vision, Chemical Senses, and Language*, American readers are again favored with a book by Professor von Frisch, the translation, by Dr. Dora Ilse, of his *Aus dem Leben der Bienen*. *The Dancing Bees* incorporates the three major topics of the earlier book with very little factual change and treats in a masterful fashion experiments on the sense of time, the general life of the hive, enemies and diseases of bees, and the origins of the colonial Hymenoptera.

The use of the word "language" to describe the movements by which bees, returned from foraging, make known the position of the foraging area to other hive residents appears to be the only point which might be a source of confusion in this clearly written book. It may be that language is used here only as a convenient shorthand term, and one ought not read too much into it. Particularly is this so because there seems to have been presented no experimental evidence that the returned worker, as it executes the direction-indicating movements, is aware that it is imparting information to other bees. Without this factor of awareness on the part of the communicator the dance of the bees is no more a language than the scents along a woodland trail are language to a dog. Were it possible to demonstrate that a returned forager bee would *not* dance without an audience, then there might be cause to label this phenomenon a language.

Complaints such as this are minor and do no particular damage to this most readable book. It remains a monument to the patient genius of Karl von Frisch and is, moreover, by no means the worst textbook ever written on the difficult art of decisive experimentation.

J. F. CASE

GENERAL PSYCHOLOGY. *Fourth Edition. College Outline Series.*

By Douglas H. Fryer, Edwin R. Henry, and Charles P. Sparks. Barnes & Noble, New York. $1.50 (paper). xx + 300 pp.; ill. 1954.

As a volume of the College Outline Series this little paperbound book is keyed to 16 leading textbooks of general psychology with widely differing approaches, including among others those by Boring-Langfeld-Weld, Munn, Ruch, Dashiell, Stagner and Karwoski, Hilgard, and Murphy.

A large part of the book is devoted to sensory and perceptual processes and to learning, including a good discussion of theories of learning. Although the present edition is announced as a drastic revision of the preceding ones, the chapter on personality cannot be considered to give an adequate picture of the status of this field in current psychology. The discussion, oriented in trait theory, considers personality only under the social aspect; problems of personality dynamics are omitted. Neither do the chapters on motives and emotions mention frustration and conflict. The chapter on tests and testing describes a large number of tests for various purposes but fails to include the latest development in the field of intelligence and differential aptitude testing.

The book will be useful for a comprehensive review of the facts and principles of general psychology before examinations. It presents the basic framework ac-

curately and clearly and can be filled in with whatever additional material or specific emphasis has been used in a course.

ANNELIES A. ROSE

PSYCHOLOGY.

By William J. Pitt and Jacob A. Goldberg. McGraw-Hill Book Company, New York, Toronto, and London. $4.50. viii + 414 pp.; ill. 1954.

This book is written with the purpose of helping the student understand his own experiences and solve practical problems as they arise in his relations with his family, his work in college, and the preparation for a career, in marriage, and in participation in the community. The approach is often a sociological rather than a strictly psychological one.

The advice given to the student in educational and vocational matters is sensible, and the problems of social stereotypes, prejudice, discrimination, and mass propaganda are handled in a straightforward manner. One wonders, however, whether the introductory chapter on the fundamentals of behavior, as well as parts of other chapters dealing with concepts and theories, are necessary, since very little reference is made to them in the later discussion of the practical problems. A treatment of theoretical constructs in such a limited space must necessarily be oversimplified and cannot give an adequate picture of the state of current psychology—especially if the presentation is often lacking in integration, as in the discussion of methods of psychological testing or of the mechanisms of solving personality conflicts, which are treated in alphabetical order.

The large number of photographs with which the book is illustrated also seems unnecessary, for the majority of them show situations with which every reader may be expected to be thoroughly familiar.

ANNELIES A. ROSE

AREAS OF PSYCHOLOGY.

Edited by F. L. Marcuse. Harper & Brothers, New York. $5.00. x + 532 pp. + 3 pl.; text ill. 1954.

The Introduction states that the purpose of this book is to acquaint the reader with the "principles, problems and procedures which are to be observed in the different areas in which psychologists are working." The book consists of 13 chapters, each by a different author, as follows: Vocational Guidance, by A. Gordon Nelson; Industrial Psychology: Selection and Placement of Workers, by Patricia Smith; Industrial Psychology: Efficiency in Work, by Thomas A. Ryan; Legal Psychology, by Harry P. Weld; Criminal and Correctional Psychology, by Raymond Corsini; Social Psychology, by Robert B. MacLeod; Child Psychology, by Lois B. Murphy and Meyer Rabban; Educational Psychology, by Frank S. Freeman; Abnormal Psychology, by Béla Mittelmann and Laura Maldenson; Clinical Psychology, by Bernard Steinzor; Physiological Psychology, by Bernard F. Reiss; Comparative Psychology, by Herbert G. Birch; and Psychology and Aesthetics, by Ralph H. Gundlach.

The book suffers from weaknesses in content as well as method of presentation. A review of the chapter headings reveals the omission of such areas as vision, hearing, and other sensory processes; nor are there any chapters on learning, intelligence testing, or personality. Certainly these are areas in which psychologists are working.

The weakness in method of presentation stems from the fact that, by and large, the authors have failed to limit their topics sufficiently so as to permit clear coverage of a segment of each field. Instead, they have attempted to cover whole fields of psychology comprehensively in about 35 pages each. In one of the chapters, for example, the author covers in a single short paragraph the psychoanalytic theory of crime (without any previous discussion of psychoanalysis), and then devotes two paragraphs to an evaluation of all psychological and sociological theories of crime.

This treatment, which is fairly typical of the book, results in a mass of rather confusing information, the usefulness of which is questionable. The chapters by Reiss and Birch on Physiological and Comparative Psychology, respectively, stand out as exceptions, in that they each present some fundamental points in their areas clearly, so that their contributions make interesting and worth-while reading. The chapter on Aesthetics, by Gundlach, is also interesting in many respects, but it too suffers from an attempt to cover too much.

The last point that might be raised relates to the usefulness of this type of book. The editor intends it as a textbook above the introductory level. It seems to me that the student who will pursue further studies in the field does not require a course of this type. Other students will gain little from any such treatment of the field.

SONIA F. OSLER

USES AND ABUSES OF PSYCHOLOGY.

By H. J. Eysenck. Penguin Books, Melbourne, London, and Baltimore. 65 cents (paper). 318 pp.; ill. 1953.

It is a commonplace experience for psychologists to find much confusion on the part of the public as to the subject-matter, methodology, and achievements of psychology. This is due partly to the failure of psychologists to inform the lay public about their activities, partly to the relative immaturity of the discipline, and

also to its rapid growth and expansion into new areas within the last fifty years. Furthermore, the popularization of psychoanalysis during the same period has produced confusion in the minds of many as to the difference between psychology and psychoanalysis. Whatever the reasons may be, it is generally agreed that the public—both the educated and the uneducated—needs to be enlightened.

This is the need that Eysenck proposes to fill in his book entitled *Uses and Abuses of Psychology*. The book is divided into four sections, each concerned with a broad area of psychology. These are: (1) intelligence testing, (2) vocational psychology, (3) abnormal behavior, and (4) social attitudes. Four chapters are devoted to each of these topics. In these chapters Eysenck discusses the methods used by psychologists, their findings, and the applications of these finds to the solution of specific problems posed by industry, education, the armed services, etc.

The exposition is clear and simple; nevertheless, there is little compromise with scientific accuracy. The result is that the reader can benefit from the book not only by acquiring a general acquaintance with the field of psychology but also by learning much useful information on specific problems.

The crucial contribution of the book is to demonstrate convincingly that psychological facts are verifiable and therefore independent of the individual psychologist or practitioner. In this sense the author contributes substantially toward an understanding of the scientific method in the social sciences.

Only one criticism might be in order. Eysenck's enthusiasm for objective tests leads him to overstate their present value, especially in connection with personality assessment. However, the many virtues of the book far outweigh this sole weakness.

SONIA F. OSLER

SCIENCE AND HUMAN BEHAVIOR.

By B. F. Skinner. The Macmillan Company, New York. $4.00. x + 461 pp. 1953.

"The hypothesis that man is not free is essential to the application of scientific method to the study of human behavior" (p. 447). Skinner's book is an argument for this viewpoint and an exposition of the picture of man that follows from such an assumption when combined with certain other assumptions about human behavior and experience. It is a surprisingly scholastic and dogmatic derivation from that set of assumptions. Only informal references are made to the scientific research of Thorndike, Pavlov, and Skinner, and without mention of specific studies in footnotes or in the form of a bibliography.

Skinner starts by equating the terms "independent variable" and "dependent variable" with the older terms "cause" and "effect." He then reminds the reader that one of the aims of science is to predict, and this means the prediction of "dependent variables" from "independent variables." "Human behavior" represents one or more "dependent variables" which the behavioral scientist wishes to predict from certain "independent variables." Skinner continually asserts that the "independent variables" are to be defined in terms of the environment impinging upon the organism from outside it. The organism itself is excluded from material contributions to behavioral occurrences; in effect, it is treated as if it were "empty." Such an assumption, however, is not in accord with the growing knowledge of the part played by spontaneous central nervous activity in the behavior of organisms.

Skinner's insistence on man's "dependent variability" to the exclusion of his "independent variability" goes to surprising lengths:

> A man may spend a great deal of time designing his own life—he may choose the circumstances in which he is to live with great care, and he may manipulate his daily environment on an extensive scale. Such activity appears to exemplify a high order of self-determination. But it is also behavior, and we account for it in terms of other variables in the environment and history of the individual. It is these variables which provide the ultimate control. (p. 240)

In effect men are no longer understood in those reciprocal relationships that G. H. Mead and H. S. Sullivan have emphasized with such concepts as "empathy" and "role-taking." The "transactions" of persons, of person and world, do not harmonize with Skinner's chosen thought-model of the scientific experiment, and so for Skinner, at least in this book, they come to seem like a bubble-like illusion which it is the bitter task of the behavioral scientist to prick. Instead, human relationships must be viewed as "cause-and-effect" relationships which are linked by the "scientific" aim of "control." From such a viewpoint, the job of the psychologist is to show how people can control or manipulate one another. Thus the book includes chapters on "shaping and maintaining operant behavior," "the controlling environment," punishment, "'self-control'," "personal control," "group control," and an entire section on "controlling agencies" in which "religion" and "psychotherapy" are included! The book closes with a section on "the control of human behavior," with chapters on "culture and control" and "the problem of control."

Skinner has performed a service by showing the consequences for man's picture of himself of an apparently absolute commitment to a limited set of assumptions for "explaining" human behavior (not to speak of "experience," which is eschewed by Skinner for scientific use). By implication if not intention, he has warned us of the possible human consequences of "under-

standing" our lives through narrowly conceived definitions of "science," "human behavior," and of the ways in which they are related. It is not incidental that the particular camera obscura view of Skinner's book is one that accords with the impersonal, conforming relationships of "the lonely crowd," the prevalence or propaganda and mass communication, and the picture of man in thought and action of totalitarian "true believers." Yet radioactive inklings of men's "independent variability" recur again and again in this Calvinism for psychologists:

> The codification of controlling practices is left to the Machiavellis and Lord Chesterfields. Psychologists, sociologists, and anthropologists usually prefer theories of behavior in which control is minimized or denied, and we shall see that proposed changes in governmental design are usually promoted by pointing to their effect in maximizing freedom. All this appears to be due to the fact that control is frequently aversive to the controllee. (p. 321)

To find an answer to the question: why this perverse human aversiveness to control? it becomes necessary to turn from preoccupation with "controlling" and "counter-controlling" in order to rediscover the forms of experienced human freedom, alone, with one another, and with the whole world of nature.

ERLING ENG

THE HUMAN BRAIN.
By John Pfeiffer. Harper & Brothers, New York. $3.75. x + 273 pp. 1955.

John Pfeiffer, a well-known member of the relatively new and rapidly growing group of "science writers" in America, here tells the story of the human brain and ancillary matters. The book speaks eloquently for what the good science writer can do. It is more than usually accurate; it is intriguing but not mysterious; it is fascinating and readable while still being intelligent and well written; and it discusses many questions with which the layman is becoming more and more concerned. What is memory? How do we think? What is mental illness? These and many other problems (the answers to which are as yet unknown) are reasonably presented. There is an admirable caution to be found in certain areas where the author has known he was on dangerously thin ice—where, for example, undue enthusiasm might make the average reader feel that more can be done by present-day therapy in mental illness than the real evidence indicates.

To be sure, there could be improvement in certain respects. The brain could have been better integrated with the rest of the organism, so that the totality of the individual and its role in behavior, psychosomatic interrelationships, etc., would have been more apparent. In certain areas of the book the emphasis could have been shifted for the better, and there are other minor questions, such as how Mr. Pfeiffer made up his mind which investigators to mention by name and which not to. On the whole, however, a vast territory bordering on the unknown and unexplored has been discussed, with, for the most part, admirable respect and restraint. The subject is remarkably difficult, and has been made understandable, in terms that will interest not only the lay reader, but many professional people as well. It should be a most valuable addition to scientific descriptive writing.

R. G. GRENELL

LA PENSÉE ARTIFICIELLE: *Introduction à la Cybernétique. 2nd Edition. L'Avenir de la Science—34. By Pierre de Latil. Librairie Gallimard, Paris.* 890 fr. (paper). 332 pp. + 8 pl. + 1 chart; ill. 1953.

In the Preface, the author of this unusual and fascinating book describes it as an adventure, the original intent of which was to present to the French public the rapidly—almost explosively—developing Anglo-Saxon science of cybernetics, a science which presented, among others, certain lingustic difficulties. As the work proceeded, however, M. de Latil continued to discover new horizons in physics, biology, metaphysics, and logic with which he became so intrigued that he could not resist the opportunity of applying the principles of automatism to broader and broader systems. He was thus ultimately led to his final generalization, namely, that, "la nature, elle aussi, est un système auto-gouverné." He refers to this idea as a "gold key" which opens a domain in which exact science is united with philosophy, in which metaphysics becomes logic, and in which virgin highways lead us to old, well-known territory. His enthusiasm is that of a hero of the Arabian Nights who wishes to take everyone to the enchanted garden despite the risks involved.

All types of automatic, self-regulating, equilibrium systems and mechanisms are described and discussed. Descriptions are given of the "turtle" of Grey Walter and the "homeostat" of W. R. Ashby, as well as of the contributions of Norbert Wiener and Warren McCulloch. The section on models is extremely interesting, and includes automatic models from the days of Descartes to the most modern constructions, such as the automatic chess player of Torres y Quevedo and various calculating machines. It is quite remarkable that this is one of the first general volumes, devoted to this most timely subject, that attempts to explain what all these systems are trying to do; in a sense, what the philosophical goal of cybernetics is, by discussing its principles in relation to thought, anticipation, memory—i.e., to the functioning of the individual, and through

that to the ultimate—the functioning of the universe in which we live.

The author is amazingly well read and presents an infinitely complex subject with a most respectable degree of simplicity. No one, for example, could possibly read this work and not understand the implications of feed-back control. It might be extremely useful to have the book translated into English so that it would reach a much wider audience. I suppose it should be mentioned that the book contains no mathematics—there is no block to understanding in the form of abstract symbols.

R. G. GRENELL

LABORATORY INSTRUMENTATION IN PSYCHOLOGY.

By William W. Grings. The National Press, Palo Alto. $4.75. vi + 282 pp.; ill. 1954.

This volume is an introduction to laboratory apparatus used in experimental psychology, and is based mainly on teaching materials the author has used in undergraduate courses in laboratory psychology. Instrumentation in animal and physiological psychology has been deliberately omitted, except for parts of a brief section on bioelectricity, so that the emphasis is on human sensory psychology and human learning.

The author offers a brief initial discussion of the role of instrumentation in psychology and then launches into a description of recording devices, including the various types of kymographs, markers, and pickups. A third chapter is devoted to devices for timing and counting. Chapters 4, 5, and 6 concern instrumentation in sensory psychology, audition, vision, and the "other" senses, respectively. The seventh chapter is on apparatus used in the study of human learning and perception; and the final chapter is the one devoted to bioelectricity and the methods for its amplification in the study of muscle, nerve, and brain potentials.

The author does a good job explaining the purpose of instrumentation, especially in his discussions of vision and audition. For many pieces of apparatus he offers pictures, wiring diagrams, and calibration procedures, as well as the names of the scientific supply houses where they may be obtained. Yet there are a number of defects in the book. First, it is restricted to commercially available apparatus and offers the reader no guide to the construction of his own apparatus or the development of new equipment. Second, the author discusses so many kinds of apparatus that he can afford no more than a brief and elementary treatment of any one. Third, while the type of apparatus discussed and the level of the discussion makes the book suitable for the undergraduate student, it is hardly more useful than a supply house catalog for the mature worker in the field. It may still have value, however, for workers from other fields who are coming into behavioral measurement for the first time, or as an elementary survey for graduate students in psychology.

ELIOT STELLAR

ART AND VISUAL PERCEPTION. *A Psychology of the Creative Eye.*

By Rudolf Arnheim. University of California Press, Berkeley and Los Angeles. $10.00. xii + 408 pp. + 3 pl.; text ill. 1954.

This book includes an introduction by the author; ten chapters entitled Balance, Shape, Form, Growth, Space, Light, Color, Movement, Tension, and Expression; 16 pages of notes; a bibliography of 326 items; and an index.

Arnheim applies to the study of art the findings of modern psychology. The format of the book is beautiful, and the volume is enriched by many pertinent illustrations. It is clear that the author has a background of familiarity both with the history of art and of psychology. He describes how the production and appreciation of a work of art is similar to the Gestalt theory of psychology, for example. The function of an element within a whole structure determines its appearance (in art) or its nature (in Gestalt theory). The mind's eye (or the mind) tries to eliminate ambiguity, disunity, or undue complication. Coherence depends on how successfully this is done. A realistic elaboration of this point is made in a developmental account of the progress of primitive or children's art from simple to more complex. But at any given stage the tendency is to simplify and unify, either in the case of observer or artist. It is helpful for us to know the perceptual reasons why we see a work of art in a certain way. Also we come to realize that art forms reflect man's own mental processes.

Since the author says in so many ways that simplicity is of the essence, one may wonder at his style of writing. Thus, the first sentence in his introduction reads, "Art may seem to be in danger of being drowned by talk." Yet there are so many side-remarks, excursions, and ideas that the book is difficult to read. Key statements are buried in unlikely places, and no very predictable arrangement of material is used within subheadings. When the author's thoughts do become crystallized, however, they are to the point. With simplification of wording and better organization, the book would be excellent reference material for art teachers and artists and for informative reading in general.

The psychological base for the book is largely Gestaltist, phenomenological, and occasionally fuzzy. It seems to be characteristic that the author starts with a kernel of hard-boiled psychological fact, but only as a landing platform for a soaring stratospheric flight into a beautiful, amorphous sky. In short, your reviewer

team of artist and psychologist agrees that this is a better book of art than of psychology.

MARION R. & ALPHONSE CHAPANIS

MOTIVATION AND MORALE IN INDUSTRY.

By Morris S. Viteles. W. W. Norton & Company, New York. $9.50. xvi + 510 pp.; ill. 1953. This book is a collection and synthesis of experimental results obtained by many investigators, primarily psychologists, of motivation and morale in a variety of industrial situations. Described, often in detail, are the methods used and the results obtained in the measurement and analysis of employee attitudes, incentives, motives, supervision, productivity, teamwork, status, etc. In addition, the volume contains an excellent account of a few concepts of social psychological theory applicable to problems of work. A complete review of pertinent psychological theory would of course be an impossible as well as an unnecessary task at this time, since research in this area is showing such great acceleration.

In 1932, Viteles wrote a textbook on *Industrial Psychology* which quickly became a classic and is unquestionably the best book on the subject ever written. There is no question that the volume on *Motivation and Morale in Industry*, published in 1953, is also without peer in the area with which it deals. These two volumes are among the most important books that the practicing industrial psychologist could possess.

This is not to say that *Motivation and Morale in Industry* has no faults, or even that it is the best psychological book on motivation. For instance, in comparison with a recent British book, J. A. C. Brown's *The Social Psychology of Industry* (Penguin Books), it shows at least one glaring weakness. In terms of usefulness, as well as general excellence, the Viteles book is far superior to Brown's. Nevertheless, there is an excellent historical and economic summary and background in Brown's book which is almost completely lacking in that written by Viteles. In his writing Viteles seems to ignore the knowledge of industrial history which he actually possesses, for the sake of emphasizing experimental results. Yet experimental results would be more meaningful if interpreted within a framework of how workers and management have come to adopt the values which they share or for which they may compete. This has been done by Brown to some extent, but not by Viteles.

The two books, different in practically every respect, are similar in their emphasis on the effect of formal and informal groups on the work of the individual. Brown, an English psychiatrist, and Viteles, an American industrial psychologist, both started their careers with an interest in the individual worker—his personality, skills, aptitudes, drives, etc.—and were apt to stress the inner capacities and drives of the individual. By the time the two books mentioned above had been written, several decades later, the writers had become impressed with the social determinants of work. It is significant that in 1953, Viteles believes that the achievement of high productivity, worker satisfaction, and industrial harmony are necessary needs of industry as well as "necessary from a broad social point of view." In 1932, he was more concerned with methods which could be used to develop the individual's potentialities.

Yet no study of productivity, motivation, and morale can afford to ignore or to overemphasize either the individual or the group. Viteles' book on *Industrial Psychology* suffered from the neglect of the broader group-setting which is essential for any complete understanding of motivation. In his new book on motivation (originally intended as a revision of one small part of the earlier work) he ignores the influences of society and historical development.

Viteles writes, teaches, and works in the city of Philadelphia, where Frederick Winslow Taylor originated the movement which brought forth the unpopular "efficiency expert" of the 1920's. The decline of Taylorism, the rise of management-labor relations, and the development of applied psychology during the expanding post World War I economy probably influenced Viteles to look for the key to increased productivity within the individual. The depression of the thirties, the impact of World War II on production, and the rise of a dynamic experimental social psychology have now apparently influenced him in the direction of seeking for a social explanation to human behavior and motivation. For instance, in his present work he has included as a reason for studying morale and motivation in industry, "the curtailment of industrial strife." This would not have occurred to him in the twenties or thirties.

A reviewer could always find many things to criticize in the best of books. To say that Viteles ignores "need" and "value" theory (surely a major omission), that he annotates excessively as if on the defensive, that he quotes more than is necessary to an understanding of the subject, and many other things of this sort, should detract in no way from the high recommendation the book deserves. Although it will go out of date as an applied textbook because of the rapid increment of experimental findings now going on, the work will always remain an unexcelled reference for the period and area it covers.

LUIGI PETRULLO

THE ORIGINS AND HISTORY OF CONSCIOUSNESS. *Bollingen Series, XLII.*

By Erich Neumann; with a foreword by C. G. Jung; translated from the German by R. F. C. Hull. Pan-

theon Books, New York. $5.00. xxiv + 494 pp. + 27 pl. 1954.

This book, the work of a prominent psychoanalytical psychologist, is an ambitious attempt to discuss the origins and history of consciousness. The book has two parts: Mythological Stages in The Evolution of Consciousness; and Psychological Stages in The Development of Personality. As Jung in his Foreword says, the author presents the ancient myths as a phenomenology of the evolution of consciousness. The myths are grouped around three main headings: the creation myth, the hero myth, the transformation myth. The creation myths begin with the "Uroboros," a symbol derived from alchemy essentially referring to a self-contained, self-perpetuating, all-possessing continuum. This state of things was before the coming of the opposites and is to be understood as the self-description of that epoch when there was no consciousness. This uroboros appears as the round "container," the maternal womb, but also as the union of masculine and feminine opposites, joined in perpetual cohabitation. The symbol, however, is essentially feminine, because man cannot think of his origin except from woman. This means that human consciousness rests finally on a matriarchal symbol. This undifferentiated feminine symbol later on changes into the Great Mother with two opposing characteristics—the good, sheltering, all-providing, tender mother, and the "terrible mother," destroying, tending to pull the weak, defenseless beginning ego back into the primordial uroboros.

The next phase in the mythology is the separation of the World Parents, in short, the birth of opposites with masculine and feminine characters represented. The male symbols play different roles. At first the males are simply phallic symbols in the service of the Great Mother, and death is their fate after fertilization takes place. This also can happen to the son. The author stresses that it is a masculine aggressive effort to get away from the enveloping uroboros of the Great Mother and to the separation of the World Parents. He equates the feminine uroboros with the darkness and the unconscious, and the masculine aggressive symbol with sunlight and the conscious.

The next great step forward is symbolized in the hero myth, with its new phase of the struggle between aggressive masculinity and the maternal possessiveness. The hero is supposed to be the son of the Great Mother with two fathers, the earthly father who does not count for much, and the God-Father who accounts for his noble birth. The hero then goes forward to combat a Dragon, which traditionally has been looked upon as a masculine symbol; in short, a symbol for the God-Father. Actually the author sees in the Dragon the symbol of the Mother and the Father, and in the slaying of the Dragon a slaying of the Father and of the Mother. Only in slaying both Father and Mother does the hero succeed in establishing himself as an entity self-possessed and in charge of his fate. According to the author, the secret of the Oedipus situation was that this was an unsuccessful revolt against mother and father because the murder of the father and incest with the mother were unconscious acts. Oedipus therefore turns out to be the prototype of the unsuccessful attempt at emancipation.

The next step is the transformation myth, in which the hero, after slaying the Dragon, captures the dragon-guarded treasure, variously pictured as his bride, pearls of great price, and so on. The hero then undergoes transformation, a transformation which in mythology means the conquest of death, since death is the primordial symbol of the decay and dissolution of the personality. This transformation is seen in the Osiris story.

The material so far is heavily documented with the myths from all ancient cultures, and just this presentation of the material alone would be eminently worth reading. The author makes an important new contribution however in this part of the book. In the gradual development of a self out of the primordial uroboros, the author, following psychoanalytical psychological teaching, calls attention to the opposite ways that the hero will react, depending upon his tendency to extraversion or introversion. Then he goes a step further and points out that there is a third tendency which feeds on and synthesizes extraversive and introversive tendencies, namely, what he calls centroversion, defined as a tendency which "makes for the development of personality and for individual realization." The object of this tendency is "the building up of a sense of the wholeness of the personality, which is an end in itself, independent of any utility value it may have."

The second half of the book has to do with psychological stages in the development of personality, and is essentially an effort to demonstrate the significance of myths for modern Western man in his personality development. The archetypal stages of Uroboros, Great Mother, Hero, and so on, are looked upon as stages in the ego's own transformation from infancy and childhood through adolescence to mature life. In an extraordinary chapter on "centroversion, ego and consciousness," Neumann defines ego-consciousness as a sense organ which perceives the world and the unconscious by means of images, themselves psychic products. Centroversion is at work as the primary function of the psyche, causing unconscious contents to present themselves to consciousness as images—first as symbolic images and secondly as the ego's reaction to them. The author sums it up in this fashion: "Centroversion is an irreducible, unitive function innate in the psychophysical structure. It produces the ego as center of a conscious system built up of contents and functions grouped around this ego nucleus." And then this provocative sentence: "It is after all scientifically justifiable to regard consciousness as one of life's experimental organs, more justifiable at any rate than to gloss over the fundamental fact of man's spiritual existence and

explain it away with reflexes or behaviorism. By postulating a creative principle at the beginning of his creation myths and placing these at the beginning of the world, man experienced his own—and by projection, God's—creativeness long before the idea of creative evolution was discovered." Centroversion, during its first conscious phase, is expressed as narcissism, later advancing to the phallic stage, which in turn divides into two elements, the lower and higher phallus, the latter representing the head end of the body and spiritual values.

Neumann defines fear as a symptom of centroversion, an alarm signal sent out to warn the ego, when the ego is in danger of regressing to an older and earlier form. The conquest of fear is the essential characteristic of the ego-hero, "who dares the evolutionary leap to the next stage and does not, like the average man who clings to the conservatism of the existing system, remain the inveterate enemy of the new. Herein lies the real revolutionary quality of the hero. He alone, by overcoming the old phase, succeeds in casting out fear and changing it into joy."

Throughout the text when Neumann touches upon the meanings of the myths, which are also the basis for some of the more fundamental symbols in Freudian psychoanalysis, he is careful to point out the traditional Freudian interpretation and the contrasting Jungian interpretation stressing the "transpersonal" meanings. For instance, the round "container," which Freud prefers to look upon as the symbol of the female genitalia in a personal sense, the author in common with other Jungians looks upon as a symbol of the brooding, all-possessing, matriarchal uroboros or Great Mother.

The reader will of course be left to choose which interpretation suits him, and I am therefore excused if, out of my own clinical experience, one interpretation seems more fitting in one case and another interpretation in another. I see nothing mutually exclusive in the two interpretations.

This book is a very valuable addition to the psychoanalytical psychological library. It is packed with facts from the world prehistory as detailed in myths, before the wisdom of which we may all be somewhat humble, and about which we might well be more conversant. This is a book not to be read once but time and again for its very valuable insights.

WENDELL MUNCIE

EMOTIONS AND BODILY CHANGES. *A Survey of Literature on Psychosomatic Interrelations, 1910–1953. Fourth Edition.*

By Flanders Dunbar. Columbia University Press, New York. $15.00. xii + 1192 pp. + 1 folded chart. 1954.

The fourth edition of this now well-known survey of literature on psychosomatic interrelationships constitutes a useful bibliography, pulled together by a psychoanalyst with interest in the relationships of personality disorders to disease. It covers the literature through 1953, and several sections which were present in previous editions have been expanded to some degree.

The book will unquestionably be of use to all those who are working in the borderland fields between the study of the emotions and the bodily changes which accompany emotional experiences, despite the fact that it is not, and as far as I can gather does not pretend to be, a critical survey. The author's major purpose was to give "a general indication of the type of material we have, where it is to be found, and where it is particularly lacking." In this, she has been successful.

R. G. GRENELL

THE ANNUAL SURVEY OF PSYCHOANALYSIS. *A Comprehensive Survey of Current Psychoanalytic Theory and Practice. Volume II, 1951.*

Edited by John Frosch and Nathaniel Ross, Sidney Tarachow, and Jacob A. Arlow. International Universities Press, New York. $10.00. xvi + 724 pp. 1954.

This second volume of *The Annual Survey of Psychoanalysis* continues the high standard set in Volume One (*Q.R.B.*, 29: 407. 1954). This is a first-rate job of combing the literature, assorting the material into topics, and integrating the material under each topic into a readable whole, with a summary at the end of each chapter. In a book with a bibliography of 276 items, it would be obviously impossible to point up the high spots, since the selection of these would depend wholly on the penchant of the reader. The chapter headings are the same as last year's and, for me, the chapters dealing with history, critique, and methodology turned out to be the most challenging. As one might expect, the history is replete with material from the Freudian letters, but the careers of August Aichhorn and Paul Federn are also discussed. In the chapter on critique, Maxwell Gitelson's paper on Psychoanalysis and Dynamic Psychiatry asserts that American psychiatry is compounded of Meyerian psychobiology and psychoanalysis. He insists that psychoanalysis is utterly different from dynamic psychiatry both in methodology and in having more inclusive goals. This not all readers may agree to, but Gitelson is entitled to his viewpoint, and one may not expect him to change his well-known position. Mitscherlich, in Critical Notes on Theoretical Problems in Psychoanalysis, examines certain fundamental postulates and definitions, for instance, the genesis of the "anal triad," proposing alternate interpretations. Similarly, Kunz, in a paper On Problem-posing in Psychoanalysis and Its Validity Within the Theory of Science, raises like questions. Mitscherlich opposes the idea of a definite anal constitution, and looks upon the child's stubborn-

ness, for example, as an attitude arising from his misunderstanding of environmental signals; in short, a way of reacting to frustration. Kunz states that "the genuine psychoanalytic libido-theoretical interpretation, which Freud characterizes by the word 'sublimation,' seems to us problematical and not convincing." Anna Freud, in Observations on Child Developments, reports from the 5-year studies of children at the Hampstead Nurseries in London. These observations confirm certain psychoanalytic theories, while others were not confirmed. In the latter group was the behavior of young children under severe trauma, for instance, after loss of parents. Regression occurred then not only to the phases of libido development, but also in the form of a loss of ego achievements. Also in this latter nonconfirmatory group it was noted that penis envy was seen in girls before two, disgust before toilet training, and shame before exhibitionism was interfered with. Masserman, in Some Current Concepts of Sexual Behavior, calls for a reorientation of traditional psychoanalytic theory in order to develop it into a more inclusive discipline relying also on relevant contributions from experimental and comparative psychologists, biologists, and sociologists. In a similar way Rado proposes that the term "libido" be divested of its pansexual implications and be equated more with Bergson's "elan vital." Milton Mazer, in An Experimental Study of the Hypnotic Dream, notes that in the elaboration and use of dream symbols there is no evidence that dream material could have a source outside of the living experience of the dreamer. Farrell, in The Scientific Testing of Psychoanalytic Findings and Theory, compares psychoanalytic theory with observational and experimental work, tending to confirm or refute the theories, and finds that psychoanalytic theory is "unbelievably bad, as *qua* theory." He finds the genetic and dynamic aspects of psychoanalytic theory only in part confirmed, and in particular he feels that psychoanalytic theory is weak with respect to the oedipal proposition. Oedipal material is often not produced in psychoanalysis. Fantasy may play a predominant role in the production of oedipal stories by adults. The oedipal theory is not necessary to account for improvement and cure. Non-oedipal theories may account for treatment consequences just as well. Levin, in The Fiction of The Death Instinct, asserts that restrictions, imposed from outside, which interfere with life and pleasure, are more significant in the origin of the fear of death than the so-called death instinct. Adelaide Johnson, in Some Etiological Aspects of Repression, Guilt and Hostility, concludes that psychoanalytic concepts concerning the relative roles of inherited drives and environment need to be drastically changed as a consequence of the observations of parents and children in treatment, and by findings of anthropologists. Such a reevaluation would affect the concepts of (1) repression as a dynamic mechanism in psychic development; (2) the meaning of restitutive behavior in a child and its association with the sense of guilt; and (3) the genesis of hostility. Waelder discusses the current theories concerning the structure of paranoid ideas and concludes that the principal feature in paranoid states is the aspect of denial, in fact, "unsuccessful denial," in analogy with unsuccessful repression in psychoneurosis as being responsible for the clinical picture.

These few samples will indicate briefly the thoroughgoing fashion in which the authors have undertaken this survey. The following chapters on Methodology, Developmental Studies, Clinical Studies, Dream Studies, Psychoanalytic Child Psychiatry, Psychoanalysis in Psychiatry, and in Psychosomatic Medicine and Theory, and Applied Psychoanalysis all continue this searching review.

This is a book to be owned, consulted frequently, and treasured for the vast amount of observation recorded therein, and for its critical attempt to survey the material.

WENDELL MUNCIE

A METHODOLOGICAL, PSYCHIATRIC AND STATISTICAL STUDY OF A LARGE SWEDISH RURAL POPULATION. *Acta psychiat., Kbh. Suppl. 89.*

By Tage Larsson and Torsten Sjögren. Ejnar Munksgaard, Copenhagen. Dan. kr. 35.00 (paper). 250 pp.; ill. 1954.

Like other Scandinavian monographs concerned with the incidence of mental disease and mental defect, this is a well-documented report which deals with a rural (insular) population living near the west coast of the Swedish mainland. The population studied consists of the inhabitants of two large and several small islands (A:bo and B:bo), altogether about 25,000 people with 1,312 mental cases registered within a period of 45 years (1900–1944). The investigative method used is referred to as the "period method," because it represents that type of a population study which covers a geographically limited area, but is extended over a prolonged period of time.

Of the elaborate census data obtained in this manner, only the first part is presented by the investigators at this time. The published account includes a discussion of the methodology, evidence for the homogeneity and representativeness of the population investigated, clinical and statistical data on the psychiatric disorders ascertained by means of available records of registration, estimates of the various morbidity risk figures for the general population, and comparative parental consanguinity statistics. The second part will deal with an analysis of morbidity rates for siblings and parents of psychotic, psychopathic, and mentally defective index cases.

Of the 763 psychotic individuals whose clinical histories form the basis for the first report, 34.2% are classified as schizophrenic; 18.1% as manic-depressive; 33% as senile, presenile, or otherwise psychotic; and 14.7% as undiagnosed. The total group of psychoses is distinguished by an excess of females (54.7%) as well as of cases falling into the categories of both schizophrenia and low-grade deficiency (10%). The general mean risk figure for schizophrenia is 1.6% for either sex; for manic-depressive psychosis, .9% for men and 1.2% for women; and for involutional (presenile) psychosis, .7% and 1.0%, respectively. The total suicide risk is estimated at 2.67% for men and at .57% for women. The rates for psychopathic personality are extremely low (.35% for men, .2% for women).

The series of 320 cases classified as low-grade deficiency (below I.Q. 55) reveals an excess of males (62.2%), general risk figures of 1% (male) and .75% (female), and a statistically significant increase from 2.6% (native population) to 4.3% (matings between first cousins) in the parental consanguinity rate. The last figure rises to 8.2% if matings between "second cousins" are included. The corresponding figures for the parents of schizophrenics are 3.7% and 5.1%, respectively.

The authors believe that the number of mental disorders that will be in need of psychiatric care will show a 1% annual increase in the period 1945–1965. Obviously, however, the validity of this estimate is limited to a rural (insular) population receiving psychiatric services of the kind which was characteristic of the period covered by this investigation.

FRANZ J. KALLMANN

A DICTIONARY OF PASTORAL PSYCHOLOGY.
By Vergilius Ferm. Philosophical Library, New York. $6.00. xii + 336 pp. 1955.

This is a dictionary of terms which the authors feel that ministers should be aware of in their religious ministry. I find it hard to assess the value of such a book. It is understandable why certain terms have been selected for representation in this book but not why some others have been selected, and why still others, full of meaning, have been left out. Much attention is paid to Freudian psychoanalysis, to the Jungian variety, to the Adlerian deviant. Nothing is said about Rank, or Stekel, or the Washington School or Karen Horney, and no mention whatsoever is made of the psychobiological school.

There are a few special signed articles—the one on parapsychology being the most startling. The signer of this article holds himself as having essentially the same feelings as expressed by S. G. Soal of London University, which he expresses as follows: "I believe that parapsychology is the most likely to provide an answer to the questions with which human beings ought to be most vitally occupied—the pursuit of happiness and the immortality of the soul. . . ."

The definitions of the scope and psychological significance of religion, sin, guilt, confession, and prayer are interesting and helpful. There are special articles on ministerial counseling and pastoral visitation that should be useful to clergymen.

The book is exceedingly annoying in one respect. If one wants to look up a certain topic, he is likely to be met with the injunction to look under another heading, and when he has chased down this second heading, he is met with the injunction to move on to something else. Consequently, he finds himself thumbing all through the book for material which ought to be more easily available.

Whether ministers will get very much of value out of this book, I frankly don't know. Psychologists won't find much of special interest in it.

WENDELL MUNCIE

THE PSYCHOLOGY OF THE CRIMINAL ACT AND PUNISHMENT. *The Isaac Ray Award Book.*
By Gregory Zilboorg. Harcourt, Brace & Company, New York. $3.50. xii + 141 pp. 1954.

This is a worthwhile book for the general reader, the lay reader in matters psychological, and those, like the lawyer or judge, who find themselves in courtroom contact with criminal psychopathology. If the author wrote this book for just such people, he did, on the whole, an estimable job. If, however, he planned this work as a profound addition to the knowledge of the psychiatrist, the psychologist, or scientist in allied fields who has even a limited understanding of psychology, he was unsuccessful.

If one can accept the viewpoint, implored on page after page, that criminal jurisprudence should look at the "individual," should learn to understand criminal motivation, and should study the psychopathology of the criminal act and punishment, then one need not spend the time required to read this book: for, essentially, this is its thesis. To expect the student of psychopathology or the student of related biological and natural sciences to be oblivious of that need, is indeed surprising. To question whether the student of the law is properly aware of this need is, perhaps, less questionable—but, in my own opinion at least, requires a more poignant and profound a treatment than is set forth here.

The most valuable material is to be found in the chapters on punishment and aggression, which include a psychoanalytic frame of reference for a psychology of aggression, to illustrate the folly (and failure) of the punitive *lex talionis*. The author defends the jury system because it is ". . . least afflicted with that narcissistic

spirit which is characteristic of the adversary proceeding under consideration." Such cavalier treatment of a controversial matter is unfortunate from so authoritative a source.

After having read that "it is only when we look into a microscope through a lens of high power that we are able to recognize certain bacteria which otherwise would entirely escape our purview" (p. 45), the reader anxiously awaited the author's recommendations only to learn that the panacea seems to reside in the institution of "qualified" forensic psychiatry. There may be some merit in this suggestion, but it does not represent a "microscopic" approach. Rather, it resembles only one additional faltering step in the direction of a more psychologically oriented jurisprudence.

HAROLD LINDNER

AN ANALYSIS OF THE KINSEY REPORTS ON SEXUAL BEHAVIOR IN THE HUMAN MALE AND FEMALE.

Edited by Donald Porter Geddes. E. P. Dutton & Company, New York. $3.50. 319 pp. 1954.

The phenomenon of the public reception of the first two Kinsey reports has receded into social and publishing history. One can hope that these important volumes may now return to the more peaceful status of careful scientific works, which is all they were intended to be. Left by the ebbing flood of public interest as a sort of residue is a large number of newspaper and magazine articles and books, the comments of scientist and layman, journalist and physician, educator and parent.

Mr. Geddes has assembled a series of such evaluations, several of them from distinguished figures. A considerable spectrum of opinion is involved. This is fortunate, and stimulating. Almost inevitably, of course, the essayists discuss not only the reports but human sex behavior itself, the mores which would regulate it, and the complications from which it is never free.

This book is uneven in quality, yet portions of it will reward the reader. The reactions to the reports are at least as interesting as the evaluations of the reports, and at several points the reader finds himself confronted with the reactions to the reactions to the reports. There are bibliographies and an index.

THOMAS R. FORBES

FEMALE SEXUALITY.

By Marie Bonaparte. International Universities Press, New York. $4.50. x + 225 pp. 1953.

This is a series of essays on female sexuality in its various aspects, as comprehended and interpreted by the psychoanalyst. The author summarizes the views of other experts in this field, and then expounds her own opinions. The developmental origin of sexuality is stressed. Because of its highly specialized nature, it is likely that this volume will be of interest chiefly to the psychoanalyst and psychiatrist. The book is well printed and includes a bibliography and index.

THOMAS R. FORBES

HUMAN BIOLOGY

BACK OF HISTORY. *The Story of Our Own Origins. By William Howells. Doubleday & Company, Garden City.* $5.00. 384 pp.; ill. 1954.

The author is primarily a physical anthropologist, but this is not his first successful venture into other anthropological fields. Here he unfolds the story of mankind through Old World and New, from earliest prehistoric times to the beginnings of the great civilizations in these hemispheres. It is easy reading, albeit the pages are packed with factual information and interpretative views. The chapter on fossil man and manlike forms reviews the evidence of man's early history and developments. He infers that *Homo sapiens* had "one definite, single source, not many, even if you wish to allow that he became somewhat mixed in different parts with remnants of rival lines. . . . It does appear as though the modern type of man goes back into the Lower Paleolithic, but the evidence is wispy." In *Mankind So Far* the author dealt in detail with prehistoric physical man, and here he devotes attention primarily to archeology and social life, with, however, a chapter on the present-day races. There are chapters on culture, language, religion, social life, forms of economic activities, and, as mentioned, of the higher cultures—Mexican, Peruvian, Egyptian, Cretan. The book is entertaining as well as informative, with sly humor and subtle wisdoms.

WILSON D. WALLIS

AN INTRODUCTION TO ANTHROPOLOGY.

By Ralph L. Beals and Harry Hoijer; with the collaboration of Virginia More Roediger. The Macmillan Company, New York. $6.00. xxi + 658 pp.; ill. 1953.

This comprehensive treatment of the field of anthropology is an excellent introduction to the topic. All major phases of the subject are presented. A portion, of 164 pages, is devoted to physical anthropology, with chapters on: Man and the Animals; Heredity and Genetics; The Criteria of Race; Fossil Man and Racial History; and Racial Types among Modern Men. These are followed by a transitional chapter on Race Problems, in which it is indicated that race, as such, has no significance for culture. The recent literature on the topics treated has been utilized, and the present treat-

ment is up to date. The account of Piltdown Man, written before the hoax was proclaimed, is prescient, and finally the puzzle is "put to one side until further data produce an acceptable solution to all the problems." Neanderthal man receives detailed treatment, following conventional lines—to some of which we would enter a demurrer, as when the authors assure us that "Neanderthal must . . . have been incapable of turning his head freely, and probably had to tilt his head backward in order fully to open his jaws." If so, he was more handicapped, or jawcapped, than the anthropoid ape. In my own opinion, what a stooping position while sitting will do to articular surfaces involved is wrongly interpreted to mean that "the posture was clearly a bent or stooping one."

WILSON D. WALLIS

THE STORY OF MAN. *From the First Human to Primitive Culture and Beyond.*

By Carleton S. Coon; line drawings by Richard Albany, photographs by Reuben Goldberg. Alfred A. Knopf, New York. $6.75. xxii + 437 + xiii pp. + 32 pl.; text ill. 1954.

This book is precisely what the title states: the drama of man the animal, and man the culture creator and bearer, from remotest prehistoric times to the present: from Adam to Atom.

It is an entrancing story, delightfully told. If you can read a few pages of this book and not finish it, you have an unusual and unenviable amount of resistance to an intellectual entertainment which is throughout informative and enlightening. Among the many highlights are the author's, arguments supporting the thesis that man, like other animals, responds physically to physiographic stimuli, as seen especially in physique: thick fat-covered bodies in the far north, small ones, and tall spindling ones in the tropical or warm climates; and an amount of pigmentation correlated, to some extent, with the amount of ultraviolet radiation. Interesting is the theory that man's evolution from early Pleistocene times has been largely a matter of the survival of the better-fitted type, rather than a development of new physical traits. In short, modern man is "as old as the Pleistocene." Some will question the generally accepted theory that man's superiority to other primates lies in his greater brain size. The author appears to be uncertain whether the anthropoid apes or the Old World monkeys are genetically man's closest kin.

Incidentally, Coon tells us more about the unknown social and economic life of Pleistocene times than any writer since H. G. Wells gave us an account of the thought and intellectual achievements of Neanderthal man.

WILSON D. WALLIS

THE BOTANY OF COOK'S VOYAGES, *and its Unexpected Significance in Relation to Anthropology, Biogeography and History. Chron. bot., Vol. 14, No. 5/6.*

By Elmer Drew Merrill. Chronica Botanica, Waltham; [Stechert-Hafner, New York]. $4.75. iv + pp. 161–384 + 14 pl.; text ill. 1954.

Plant geography is rife with hypotheses dealing with the trans-Pacific migration of plants, in particular those which may have served as food and hence as indicators of migrating peoples. Basing his conclusions on unpublished work of Solander, who accompanied Cook on his first voyage, on the studies of the Forsters, who were on the second voyage, and on his own vast knowledge of Eastern flora, Merrill states that the Society Islands had only one American food plant, the sweet potato, and possibly several weeds of similar origin which existed prior to the European exploration period. He vigorously argues that the peoples of Malaya brought in other species.

Merrill makes short work of those who disagree with his concepts of plant distribution and migration. Heyerdahl, Carter, and Sauer are subjected to a merciless dissection, and, it would seem to me, an uncalled-for and highly personalized castigation. On the other hand, and apart from the vindictiveness of Merrill's handling of the ideas of others, few can dispute Merrill's familiarity with the Pacific flora, and his interpretations will have to be taken into account by those who would utilize the data of plant distribution to support their own ideas of plant origins and human migrations.

C. P. SWANSON

THE HUMAN MASTICATORY APPARATUS. *An Introduction to Dental Anthropology.*

By Meyer Klatsky and Robert L. Fisher; foreword by Wilton Marion Krogman; introduction by Leuman M. Waugh. Dental Items of Interest Publishing Company, Brooklyn; Henry Kimpton, London. $6.00. xxiv + 246 pp.; ill. 1953.

As pointed out by Wilton M. Krogman in his Introduction, this book is planned to awaken the average practicing dentist to the importance and significance of his limited area of study to the body and to the individual as a whole. Since almost everything in the area of dentistry may be drawn under the canopy of "Anthropology," it is not surprising that the authors have chosen for consideration certain of the more interesting and obviously anthropological facets of dental knowledge. Naturally, such a work must be largely one of review and recapitulation of the works of many investigators. Each chapter has its own short bibliography, and there is a glossary of terms judged by the authors to be unfamiliar to some among their prospective readers. The chapters on Evolution and Dental Degeneration,

Factors Influencing Growth and Development, Dental Anthropology, Effect of Diet, Malocclusion, and The Relation of Genetics to Dental Science, offer interesting introductions to their respective fields of thought. Equally interesting, but not so well integrated to the general theme, are chapters on the Causes of Dental Caries, its Incidence and its Prevention, Periodontal Diseases, and Dental Anomalies. The essays on Dentistry as a Public Service, Biological Dental Restoration, and The Future of Our Third Molars seem not to belong specifically to the other material. The book meets the first of the basic objectives of a specialty publication, in that it is fitted to its primary group of prospective readers.

JOHN A. CAMERON

THE PREVALENCE OF PEOPLE.

By Marston Bates. Charles Scribner's Sons, New York. xvi + 283 pp.; ill. 1955.

On a particular afternoon in 1948, the then director of the International Health Division of the Rockefeller Foundation suggested that entomologist Marston Bates transfer his interests and apply his biological training to a new field. Bates had made major moves before: from economic entomology for the United Fruit Company in Honduras and Guatemala, to a doctoral dissertation on the butterflies of Hispaniola, to field study of mosquito-borne diseases and their vectors in Albania and Colombia. This time the subject was to be the population problems of mankind—once more under Rockefeller auspices. Bates began to call himself a "human ecologist."

The Prevalence of People is a popular summary of his personal thoughts on the subject, dealt with "at the cocktail party level." It delves shallowly but delightfully into the numbers, nature, and kinds of mankind, man's means of subsistence, his reproductive habits and attempts to control them, his causes of death (whether war, famine, or disease) and success at postponing death, his migrations and their effects. The style chats along in the first person singular, with many a humorous twist that is pure Bates. The comments are bolstered by 22 pages of notes and references, and end with a good index. For those who find William Vogt too startling, Fairfield Osborn too general, Harrison Brown too specific, Bates' book should have particular appeal.

LORUS J. & MARGERY MILNE

POPULATION STATISTICS AND THEIR COMPILATION. *Revised Edition.*

By Hugh H. Wolfenden; with an appendix on Some Theory in the Sampling of Human Populations, by W. Edwards Deming. Published for The Society of Actuaries by The University of Chicago Press, Chicago. $7.50. xxiv + 258 pp.; ill. 1954.

This book is a description of the source and compilation of vital statistics: the methods of securing numbers of persons, births, deaths, marriages, and their characteristics. The contrast between the census and registration processes is clearly drawn, and the use of each for specific types of data is discussed. Special attention is given to the procedures in the United States, Canada, and Great Britain. Accompanying each description is a consideration of the errors involved and necessary precautions in using the figures. The author is writing primarily for actuaries, so that the construction of mortality tables is the major application of the material. A number of other sociological problems, such as population forecasts, orphanhood, unemployment, illness, and reproductive rates receive brief treatment.

This second edition comes 29 years after the first. The essential structure and purpose of the book remain unchanged, but there is a wealth of new material in each of the 13 original chapters; and 2 new chapters are added, one on forecasting mortality rates, the other on the theory of reproductivity. The Appendix, by Deming, who is a specialist in the field of population sampling, is a very valuable addition, presenting briefly several of the sampling procedures which have been largely developed and applied since the first edition appeared.

The book does not undertake to deal with some of the general "population problems" but does the job that students of these problems depend on, an examination of the source material. It is thus a valuable reference book for students in any field requiring population data. The text is liberally sprinkled with references to the literature on basic data, methodology, further elaborations, and other applications. These are not presented in a systematic bibliography, so that it is not easy to judge their completeness, but there seems to be some neglect of references to pertinent work by the Expert Committees of the World Health Organization and by the Population Division of the United Nations. There is no index. As far as subject matter is concerned, the very detailed Table of Contents may serve this purpose; but an index of names would enhance the usefulness of the book, particularly in locating references.

In the decades since the appearance of the first edition, there has been an intensive development of interest in demography as such, as well as in the many fields of study depending on population data. The revised edition of this useful reference is timely and welcome.

MARGARET MERRELL

COHORT FERTILITY. *Native White Women in the United States.*

By Pascal K. Whelpton. Princeton University Press, Princeton. $6.00. xxviii + 492 pp.; ill. 1954.

One of the outstanding events in the recent demographic history of the United States has been the increase of the birth rate from 18.6 per 1,000 population in the quinquennium 1933–37 to 24.7 per 1,000 in 1948–52 (adjusted for underregistration). The classical gross reproduction rate rose even more steeply, from 1.09 to 1.55. This "baby boom" led many observers to proclaim the reversal of the secular trend toward smaller families and to anticipate spectacular rates of population growth for the remainder of the century.

In this situation, P. K. Whelpton's monumental study of cohort fertility is one of the most important contributions to demographic literature. There is little doubt in my own mind that cohort analysis will prove to be a long step forward in our understanding of the dynamics of population growth.

The term "cohort" is used by demographers to designate a group of persons or couples simultaneously entering statistical observation and followed over a period of time. Whelpton uses birth cohorts of native white women in the United States, i.e., groups of women born in successive years from 1875 to 1933 (British demographers have used marriage cohorts, i.e., groups of couples married in successive years). The older birth cohorts can be followed to the end of the childbearing period (assumed to be age 47), by which time their completed fertility can be recorded. More recent cohorts cannot be followed to the end of the childbearing period, but the numbers of children born to them by a given age can be compared with the cumulated fertility of other cohorts up to the same age. Where the requisite basic data are available, as in the United States, similar calculations can be carried out separately for first, second, third, and higher order births.

With the aid of an impressive and skilfully marshalled array of statistical tables Whelpton demonstrates that completed fertility has declined from 3.576 births per native-white woman in the cohort of 1875 to 2.446 births per woman in the cohort of 1903. More recent cohorts had not reached the end of the childbearing period in 1950, the last year for which data were available, when the calculations were made. The numbers of children born to these later cohorts up to specified ages (40, 35, 30, 25) follow consistent upward trends, with a maximum relative increase of 38% recorded at age 25 for the cohort of 1925 as compared with that of 1915.

It is shown, however, that the upward trend of (incomplete) fertility among the more recent cohorts has to a large extent resulted from the making-up of marriages and births which had been postponed during the depression of the 1930's and from a tendency to marry at an earlier age. Further analysis (see also Whelpton's article on "Future Fertility of American Women" in the March, 1954, issue of the *Eugenics Quarterly*) suggests that completed fertility will reach a minimum of about 2.3 births per woman in the cohort of 1909 and will then increase. The extent of the anticipated increase is, however, much less steep than one might be led to believe on the basis of crude birth rates or classical gross reproduction rates. In the main, this increase in completed fertility will be accomplished by a relative reduction in the numbers of childless families and of families with only one child. The incidence of really large families will almost certainly continue to decline, and the United States will remain a nation of controlled fertility.

Whelpton is now engaged in studies that will eventually extend the available body of data on cohort fertility from native white women to all women, will improve techniques of assessing the future reproductive performance of recent cohorts, and will apply to the problems of making population projections a new insight into the dynamics of fertility.

CHRISTOPHER TIETZE

EROTIC ASPECTS OF JAPANESE CULTURE.
By Lawrence E. Gichner. Published by the author, 3405 Woodley Road, N.W., Washington, D. C. $10.00. 94 pp. 1953.

Erotic art and literature exist in many cultures of the world, often in highly institutionalized patterns. While these activities may be entirely overt in their original environment, research and study are hampered by our own institutions which relegate them to the realm of the clandestine.

Erotic Aspects of Japanese Culture, a slender volume of 94 pages, is the second in a series of studies of erotica to which the author has devoted himself for many years. Like its predecessor, *Erotic Aspects of Hindu Sculpture*, it maintains a refreshingly frank, but at the same time dignified, approach toward a subject on which all too little systematically organized information is available. As L. E. Gichner himself states, this book might be called "a primer, a first reader, to impress the serious students with the idea that it is not an exhaustive study and that there exists both ample material, and also the need, for further sober researches and specialized studies."

The book is "privately published for use and study by scholars in the field of anthropology, and in the social sciences; by physicians, psychologists and psychiatrists." It contains many fine and carefully chosen examples of scrolls, woodcuts, sculptures, and other representations, as well as selections from literature, dealing with the sexual organs and the act of reproduction. The author points out that "the Japanese are a beauty-loving people and portray the creative act with skill, originality, finesse, dignity, and occasional humor." Indeed, it is the combination of thoughtful analysis and appreciation of aesthetic values that lends

to this little book its own originality, making it both readable and instructive.

CHRISTOPHER TIETZE

CONSERVING NATURAL RESOURCES. *Principles and Practice in a Democracy.*

By Shirley W. Allen. McGraw-Hill Book Company, New York, Toronto, and London. $5.50. ix + 347 pp.; ill. 1955.

This textbook arose for a common reason among college-level works: an instructor's continued dissatisfaction with existing books. As such it strives (1) to achieve unity of approach, because of single authorship, and (2) to include nonrenewable resources as well as renewable.

The writing is spare and follows a conspicuous outline, strongly suggestive of expanded lecture notes. The principal treatment of nonrenewable resources is the sixth, The Mineral Resources, of 7 chapters in the book; it occupies 63 pages. The final chapter, Human Powers as Natural Resources, is accorded 10 pages. The atmosphere is treated briefly as an inexhaustible resource, and radioactivity is mentioned only in connection with the single-page treatment of uranium, radium, and thorium; fall-out and disposal of radioactive wastes are omitted, along with war as a factor affecting mankind.

A student reading the book might easily conclude that plankton organisms were exclusively marine and are important chiefly as food for California sardines, that the only economically significant insects were those attacking forest trees, and that the only invertebrates of importance to man were clams, crabs, lobsters, shrimp, and sponges. The basic concept of a pyramid of numbers seems to have vanished under a mound of pumice and pumicite. Concern over "harmonious property relations" takes the place of a clear statement of the need for intelligent and informed cropping of resources. The volume encompasses many aspects of the subject—physical, technical, legal, political, economic, social, and human. It is short on good ecology and any conviction of the urgency for man to get into balance with his environment.

LORUS J. & MARGERY MILNE

BIOMETRY

STATISTICS AND MATHEMATICS IN BIOLOGY.

Edited by Oscar Kempthorne, Theodore A. Bancroft, John W. Gowen, and Jay L. Lush. The Iowa State College Press, Ames. $6.75. x + 632 pp.; ill. 1954.

The contents of this volume are the contributions of no ess than 46 well-known statisticians, biometricians, biologists, and geneticists, who, with many others, assembled in Ames, Iowa for the Biostatistics Conference in the summer of 1952. Naturally, a very large variety of topics has been covered, ranging from curve fitting and the philosophy of experimentation to cattle twins and nucleoproteins in cell division. Most of the papers give a review or introduction and a discussion of the subject under consideration plus whatever new developments have been obtained to date. Some others may be considered original research papers that might be published as such in professional journals. The 44 papers are broadly grouped into five parts: Principles and Procedures; Competition Problems; Estimation of Populations; Bioassay Problems; and Population and Radiation Genetics. Readers should be warned that these section titles are inadequate to indicate the contents of the individual papers (which are too many to be listed here). A volume like this clearly shows what a fertile field of research for statisticians and mathematicians biology is.

Although perhaps no biologist is expected to be conversant with every topic discussed, this volume will undoubtedly be a most valuable reference work for a large number of professionals: animal and plant breeders, ecologists and geneticists, as well as demographers and "pure" statisticians. It can also be used as a source book for teachers. For graduate students who have had some basic biology and elementary statistics, it can be used for seminar courses to get them acquainted with some advanced problems in their chosen fields.

More than 900 references are listed in the Bibliography. There is a very complete index (16 pages). Excellent editing is shown by the rarity of typographical errors. However, one of these is in the reviewer's own name in the Bibliography.

C. C. LI

DE OMNIBUS REBUS ET QUIBUSDAM ALIIS

CONCISE SCIENCE ENCYCLOPEDIA.

Contributors: C. L. Boltz, S. S. B. Gilder, J. T. Hogg, T. J. Morgan, D. Rieser, Walter Shepherd, Paul I. Smith, K. R. Wallace; edited by G. E. Speck. Thomas Y. Crowell Company, New York. $3.50. 256 pp. + 31 pl.; text ill. 1954.

The jargon of the scientist becomes increasingly complex with the passage of time and the expansion of knowledge. The inevitable effect is to widen the cleavage between those who speak the language and those who do not. Yet an understanding between the scientist and the layman is necessary for a sympathetic appreciation of what is being done in the way of research and its implications to society. This volume should help to lessen the gap, for it is only through

words that mutual understanding and respect are achieved and a proper perspective is gained. All phases of science, both applied and basic, are touched upon, and by means of illustration and definition, many hundreds of terms and phenomena are explained. A spot check of approximately 100 biological terms indicates that the volume can be put to good use, and that the definitions and explanations are concise, clear, and adequate.

C. P. SWANSON

PHOTOGRAPHING YOUR FLOWERS. *A Practical Guide for Indoor and Outdoor Use.*

By John P. and Mary Alice Roche. Greenberg Publishers, New York. $3.75. viii + 152 pp.; ill. 1954.

The title accurately describes the contents of the book. The Roches have freely illustrated the text with their excellent photographs, chosen as examples of the subjects discussed. There are sections on prearrangement of the garden, lighting, allowance for foreshortening, and methods for interior photography. The authors are obviously experts in their field, and probably this will be a useful book for the professional or very accomplished amateur photographer, that is, for the persons who already know and understand those familiar subjects, "composition" and "arrangement" in photography. But for the ordinary or even good photographer, the bulk of the material is of little use, simply because the artistic concepts of composition, the principal concern of the book, are not adequately expressed in words.

ALAN D. CONGER

AN ATLAS OF ANATOMY FOR ARTISTS. *Second American Edition.*

By Fritz Schider; revised by M. Auerbach and translated by Bernard Wolf; new bibliography by Adolf Placzek; additional illustrations mainly from historical sources. Dover Publications, New York. $6.00. xxiv + 163 pl. + iii pp. 1954.

The first American edition of this German classic atlas was a much welcomed friend to artists and sculptors of the human figure. This second edition surpasses the first because of the following new features: (1) a collection of inspiring sketches by such time honored men as Vesalius, DaVinci, Goya, and Michelangelo; (2) a male and female subject, each photographed from front, back, and side from age 4 through 18; (3) action studies of adult male, female, and child from the Muybridge series; and (4) a bibliographic guide.

Several very dated photographs which had reproduced poorly and which were inferior in composition have been omitted from this edition. The book sticks to its subject and might well be called the final court of appeal where problems concerning human figure drawing are concerned.

WILLIAM E. LOECHEL

THE MICROTOMIST'S FORMULARY AND GUIDE.

By Peter Gray. The Blakiston Company, New York and Toronto. $10.50. xiv + 794 pp.; ill. 1954.

Consideration of the adequacy of a volume on microtechniques naturally revolves around the completeness with which coverage is given to those aspects of the subject familiar to the reviewer. Cytology is given but cursory attention, and even the aspects covered are likely to lead to rather disappointing results in the hands of those who would use them for modern problems. Indeed, the general philosophy of the volume, if one may be permitted to read between the lines, is that of classical and descriptive biology rather than that of the more modern experimental approach. Not that the techniques of the past cannot be put to present use, but that in describing them at least reference to their use in experimental problems could be made. As to this point, and by way of illustration, little or no space is given to the methods and techniques of histochemistry or cytochemistry, or of electron microscopy and its special problems of fixation and embedding, with the consequence that the methods section of the volume will be principally of use to the histologist, anatomist, and embryologist. The formulary section, however, is quite complete, and stain preparations and literature citations are most extensive and detailed.

One may well be appalled by the vast amount of work going into the preparation of such a volume as this. Necessary though these are for the researcher to ply his trade, there are few who would have the temerity to undertake such a task and see it through to completion. The author must be accorded praise for his perseverance.

C. P. SWANSON

BIOLOGICAL APPLICATIONS OF FREEZING AND DRYING.

Edited by R. J. C. Harris. Academic Press, New York. $10.00. xii + 416 pp.; ill. 1954.

The past war witnessed the full-blown application of a technique which had been known for many years but which had rarely been of more than limited importance. The need for blood plasma in particular led to an immediate appreciation of the significance of the techniques of freezing and drying, and the usefulness of these processes is now familiar to everyone. Freezing, followed by drying in vacuo, has a far wider application,

however, and biologists have not been slow to make use of the technique in their own investigations. Apart from the medical value of freezing-drying in the preservation of blood fractions, antibiotics, and foods, the utilization of the methods in virology, bacteriology, electron microscopy, and tissue culture studies has been in the nature of a revolution. The present volume deals with the application and the results of freezing-drying in a variety of ways, and the 14 chapters are written by authors whose work in these areas is well known. Much of the substance of the book is methodological, but the treatment considers also the possibilities for future research as well as the immediate results from such work as has been done. The usefulness of the book is therefore not limited to a particular field of research, but spreads into a variety of biological disciplines.

C. P. SWANSON

SCIENCE NEWS 33.
Edited by A. W. Haslett. Penguin Books, Melbourne, London, and Baltimore. 50 cents (paper). 128 pp. + 16 pl.; text ill. 1954.

Out of 7 major articles in this number of *Science News*, which is always interesting, only 2 articles pertain to the biological sciences: Instinct and Learning, by S. A. Barnett; and Recent Work on Bacteriophage, by J. E. Hotchin. Biologists will also be interested in the article by G. H. Drury on Weather, Climate, and River Erosion in the Ice Age.

However, it is not unlikely that biologist readers of magazines like this and the *Scientific American* are more often attracted to the non-biological articles. Here they may broaden their general perspective through reasonably non-technical yet sound articles on a great variety of scientific subjects. This number includes, for example, articles on High-Energy Nuclear Disintegrations, Celtic Interlacing Patterns and Topology, Fire Research, and New Ways of Taking off and Landing. Perhaps the preponderance in numbers of biologists among scientists and of biological papers in the scientific literature is the reason for the opposite balance in the fare of reading matter in magazines of this type.

The brief Research Reports, Correspondence, and some comments on Books Received complete the issue.

THE QUARTERLY REVIEW OF BIOLOGY publishes critical reviews of recent researches in all of the special fields of biological science. The contribution should present a synthesis or digest of the researches and a critical evaluation of them. A mere synopsis of the literature without evaluation or synthesis is not desirable.

Theoretical papers are published occasionally, especially when such papers (1) include a critical synthesis of the literature bearing on the theory and (2) are likely to promote further research in a given field.

The article should be written in concise language, yet in sufficiently non-technical form as to be intelligible not only to specialists in other fields but to the general biologist as well. To this end the article should have a general introduction and a summary which enumerates one by one all of the principal facts and conclusions given in the paper. Interpretative diagrams and schemes are very desirable.

Material ordinarily taking the form of footnotes is set in small print and placed in the text and consequently should be written in a style so as to fit readily into the text. Acknowledgments are printed in the text in small type at the end of the article just preceding the List of Literature. Recent issues of the Quarterly should be examined for style as regards (1) section or subsection headings in the text, (2) literature citations in the text, and (3) List of Literature.

The subjects and authors of articles are selected by the Editors and members of the Advisory Board. Unsolicited articles which conform with the objectives of the Quarterly will be considered for publication.

A feature of the REVIEW is the section dealing with *New Biological Books*. In this department the book literature of different countries in the field of Biology is given prompt notice.

The QUARTERLY REVIEW OF BIOLOGY is issued in March, June, September and December.

Twenty-five reprints, with covers, of articles will be furnished to contributors free of cost. The reprint order blank accompanying galley proofs gives the cost of additional reprints.

Manuscripts may be sent to Dr. B. H. Willier, Department of Biology, The Johns Hopkins University, Baltimore 18, Maryland.

Books for Review may be sent to Dr. H. B. Glass, Department of Biology, The Johns Hopkins University, Baltimore 18, Maryland.

New subscriptions and renewals are entered to begin with the first issue of the current volume. Should any issue of the current volume be out of print at the time the subscription order is received, the pro-rata value of such numbers will be refunded to the subscriber.

Subscriptions should be renewed promptly—To avoid a break in your series, subscriptions should be renewed promptly. The publishers cannot guarantee to supply back issues on belated renewals.

Subscription price: $6.00 United States. Countries within the Postal Union and foreign countries, $6.75; Canada, $6.25. Single copies will be supplied, when available, at the rate of $1.75 a copy, plus $.25 postage outside USA.

Claims for copies lost in the mails must be received within 30 days (domestic).

Change of address—Publisher must be notified 60 days in advance. Journals undeliverable because of incorrect address will be destroyed. Duplicates can be obtained (if available) from the publisher at the regular price of single issues.

THE WILLIAMS & WILKINS COMPANY

Publishers of Scientific Books and Periodicals

BALTIMORE, U. S. A.

CONTENTS

The Etiology of Crown-gall
—*Richard M. Klein and George K. K. Link* (207–277)

New Biological Books
An Empire of Learning
—*Edward H. Hume* (278–280)

Reviews and Brief Notices (280–330)